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SUBTEMPORAL AND SUBOCCIPITAL MYOPLASTIC CRANIOTOMY

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In no branch of surgery is the maneuver of opening and closing the wound more important or more arduous than in cranial surgery. We desire to describe a simple operative technic which in our hands has proved to be superior to the conventional subtemporal and suboccipital procedures.

MYOPLASTIC SUBTEMPORAL CRANIOTOMY

The myoplastic subtemporal craniotomy technic permits rapid exploration through a wide unobstructed opening and provides a firm, safe restoration. The steps of the procedure follow in detail.

1. A curved incision, as indicated in the insert in figure 1, is made in the scalp without wounding the pericranium. This incision skirts the superior temporal line to which the fascia of the temporal muscle is attached. This ends anteriorly at or just behind the hair line. Posteriorly the incision is swung slightly forward on the supramastoid crest, which lies at the level of the superior border of the zygoma. The superior temporal line is identified anteriorly by palpation. It is a direct continuation of the prominent temporal ridge of the frontal bone. As this incision is deepened, the pericranium is exposed just beyond the temporal muscle fascia. The incision so outlined is within the hair line, it permits maximum exposure, and an incision is not made in the temporal muscle. By palpation the extent of the temporal muscle fan can be outlined quickly by having the patient bite.

2. The scalp flap is reflected from the periosteum until the temporal fascia attached to the superior temporal line of the parietal bone and

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Such words as "histologic" and "anatomic" are used in this article only in order to conform to the nomenclature which is compulsory for publication in the ARCHIVES OF NEUROLOGY AND PSYCHIATRY. The authors would prefer the words "histological" and "anatomical."

the posterior part of the temporal ridge of the frontal bone is exposed. An incision is carried down to the calvarium through the line of fascial attachment, and the muscle and scalp flap are reflected from the temporal bone and retracted with two or three guy sutures attached to rubber bands (fig. 1).

3. The bone is removed from the temporal fossa up to within a centimeter or less below the fascial incision. An opening 9 by 7 cm. is thus readily obtained, which will still permit satisfactory repair (fig. 1).

4. To reattach the myoplastic flap, holes are made in the margins of the bone defect, usually from twelve to fourteen, and interrupted chro-

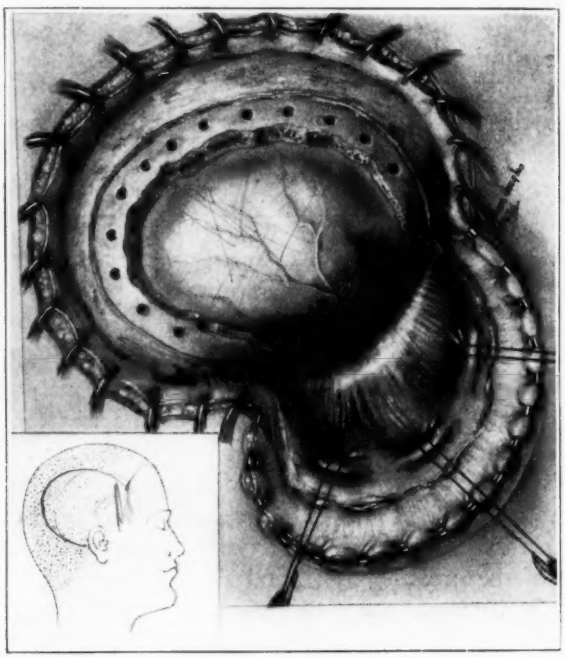

Fig. 1.—The incision in the scalp is outlined in the insert. The dura has not been opened, but the location of the sylvian fissure is evident. On the side of the flap hemostasis has been obtained by Michel clips. The flap is retracted by guy sutures attached to rubber bands.

mium steel wire [1] sutures, size 33, are passed through the holes and up through the muscle and overlying fascia and are tied next to the bone (fig. 2).

1. Babcock's chromium steel wire (J. A. M. A. **102**:1756 [May 26] 1934) is superior to silver wire, catgut or silk for this purpose and when buried in muscle seems, according to our preliminary histologic studies, to give rise to less reaction than any other material. When silk is used for bone sutures a good deal of foreign body reaction results, much more than when silk is buried in soft tissue.

5. The fringe of fascia and pericranium left attached to the flap as it was reflected is sutured either with interrupted silk sutures or with a continuous locked silk suture, and the scalp is closed in two layers, as usual (fig. 2).

Comment.—We have found that this procedure gives a considerably wider exposure of brain than the muscle-splitting operation (fig. 3). It is entirely adequate for the unobstructed removal of a tumor of the temporal lobe or for exploration in a case of bleeding of a meningeal artery, and it is possible to leave a large decompression when indicated. It has been our custom to close the upper portion of the dura so as to

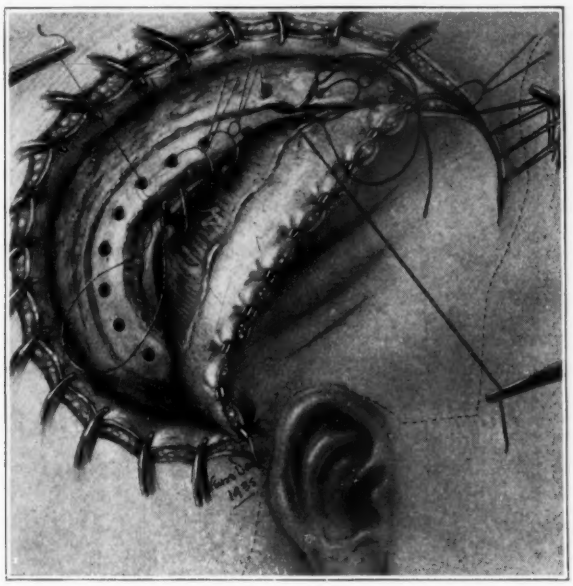

Fig. 2.—The closure is in four layers. Chromium steel wire is used to attach the muscle to the bone. Silk sutures, either interrupted or continuous, close the pericranium. The galea is closed either with continuous locked silk sutures or with interrupted silk sutures. The skin is closed with dermal sutures taken continuously and locked.

hide the fissure of Sylvius, allowing only the temporary lobe to protrude against the muscle when a decompression is to be left on the dominant side, in order to avoid herniation of the speech area.

It is obvious that when wide exposure is unnecessary the incision and opening in the bone may be modified as desired.

MYOPLASTIC SUBOCCIPITAL CRANIOTOMY

This procedure may be used for either a bilateral or a unilateral exploration of the posterior fossa. It has been our custom to reflect

the flap from the entire occipital bone in most instances, even though the opening in the bone is to be on one side. When there is to be bilateral exposure of the bone, an incision in muscles is not required, and should it become necessary during a unilateral exploration to extend removal of the bone to the other side it can be done quickly.

1. The incision (fig. 4 *A*) extends from the level of the tips of the mastoid processes to a point from 4 to 5 cm. above the external occipital protuberance. The lateral wings of the incision are so placed that the muscles of the neck attached to the mastoid process will not be cut, the incision coming down through the occipitalis muscle directly to the peri-

Fig. 3.—A roentgenogram taken postoperatively, showing the opening in the skull through which a large infiltrating glioma of the island of Reil was removed. The holes and steel wire suture by which the muscle was reattached to the skull are at the margin of the bone defect.

osteum of the mastoid bone. The point at which the lateral incision is to be made may usually be determined by palpation of the mastoid area. In figure 4*B* the incision is 2.5 cm. from the point at which the lobe of the ear is attached to the scalp. Palpation had demonstrated that the attachment of the muscles of the neck was mesial to the site of incision. In some instances it is necessary to swing the incision even farther laterally to avoid the muscles of the neck.

The incision in the scalp (fig. 5) includes the galea but not the pericranium. The upper concave edge of the incision may be separated

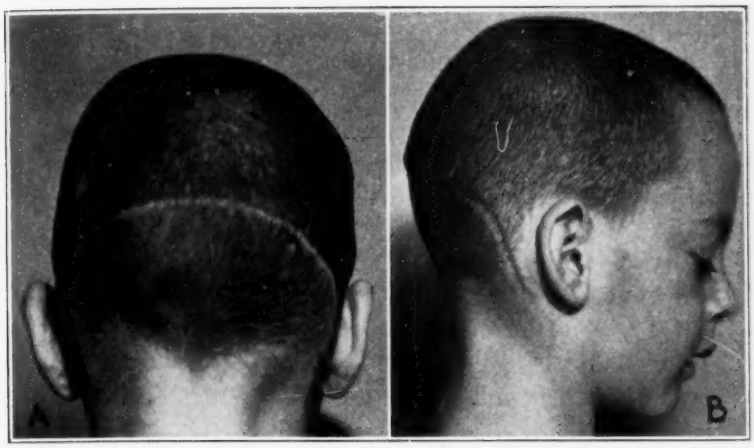

Fig. 4.—*A* is a photograph of the wound eight days after operation, showing the incision and satisfactory anatomic restoration. *B* is a lateral view, showing the position of the incision over the mastoid process.

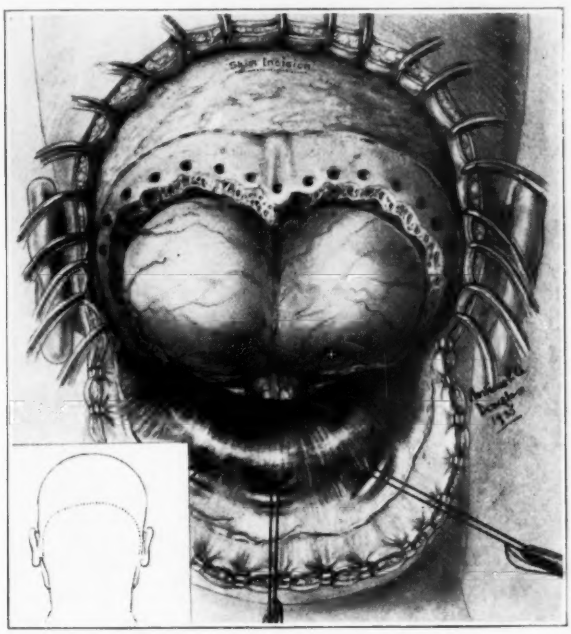

Fig. 5.—The suboccipital exposure, with the insert to show the incision. The posterior arch of the foramen magnum is removed, and the arch of the atlas has been taken away. An incision has not been made through the muscle. The muscle is left entirely attached to the overlying scalp. Exposure of the lateral sinus may be more extensive than is shown and still permit safe restoration.

from the pericranium in an upward direction to allow the bur holes to be made for ventricular puncture.

2. The scalp flap is reflected downward as far as the external occipital protuberance. The pericranium is then incised, and while the flap is being retracted the suboccipital muscles are elevated from the bone down to the foramen magnum. The fact that the lateral margins of the incision are carried to the tips of the mastoid processes permits the reflection of the flap, so that it is easily possible to expose the spines and laminae of the two upper cervical vertebrae. The whole flap is held out of the way with guy sutures attached to rubber bands.

3. Removal of the bone is carried down to the foramen magnum and upward so as to expose the transverse sinus as desired. The entire sinus may thus be exposed, and satisfactory restoration can still be

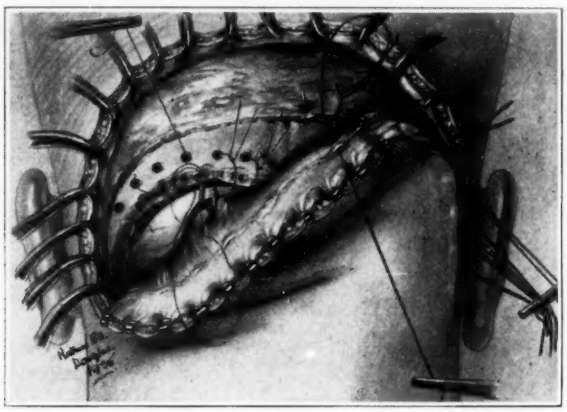

Fig. 6.—As in the subtemporal technic, the closure is in four layers, i. e., muscle to bone, periosteum, galea and skin.

obtained. Indeed, removal of the bone has been frequently carried high enough to permit ligation of the sinus, section of the tentorium and elevation of the occipital lobe, a maneuver which has been so effective in the hands of Dr. Max Peet.

4. At closure (fig. 6), in order to reattach the reflected myoplastic flap, from fourteen to sixteen holes are made in the margin of the bone defect about 1 cm. apart. The point at which the muscle layer begins on the ventral surface of the flap is, of course, obvious. Babcock's rustless steel sutures are passed through the holes, through the muscle and its aponeurosis, and then tied next to the bone. The fringe of pericranium left attached to the flap is then sutured, and the scalp is closed in two layers as usual. Except for the steel wire used to attach the muscles to the bone, silk is used for the buried sutures.

When drainage is instituted, rubber dam tubing of small size is carried out through a separate stab wound at some distance above the incision. The long tract makes it possible to stop drainage of cerebrospinal fluid at once by pressure when the drain is removed.

Comment.—The incision can be so planned that no muscle is incised, which greatly decreases bleeding. The only vessels cut across in this myoplastic type of exposure are those in the scalp and the usual emissary cranial veins always opened during exposure of bone in this region. The restoration of muscles made possible by this method is so firm that elaborate immobilizing dressings are unnecessary. This compact closure of muscle to bone and suture of the pericranium prevents troublesome postoperative accumulation of fluid.

We have had various opportunities to study the myoplastic suboccipital restorations at second operation and at autopsy. In every instance the plastic result was entirely satisfactory from all standpoints. Two instances may be described. In the first case the myoplastic suboccipital procedure was used to carry out a cerebellar exposure. A tumor was not observed, and the dura was left open for decompression. Following the operation headache and vomiting ceased, and papilledema subsided. Signs recurred, and the decompression became very tense but could not bulge. A second suboccipital exposure was easily accomplished six months after the first through an anatomically perfect area of repair. The tumor arising from the pineal body and projecting beneath the tentorium was verified but was not removed. The sequence of events is given in this detail to show how effectively the plastic repair at the first operation withstood the increased pressure caused by a blocked ventricular system and to show that reopening of the wound was not difficult.

In the second case a fifty-seven day old area of plastic repair was studied at autopsy. An acoustic perineurial fibroblastoma on the left side was removed from a patient who was also suffering from essential hypertension. The operative wound healed well, and the patient left the hospital on the seventeenth day. Unfortunately, however, she died forty days later of an overwhelming cerebral hemorrhage. Figure 7 is a photograph of the specimen removed at autopsy and shows the occipital bone above and the diaphragm of reattached muscle and fascia below. On the right the tissue has been scraped off to show the drill holes. Chromic catgut suture had been used to attach the muscles to the calvarium through the multiple drill holes. The sutures themselves had completely absorbed. The drill holes were filled with firm cylinders of connective tissue, binding the flap to the bone, and the muscle was bound to the edges of bone around the bone defect, giving a permanently strong reattachment.

Wider exposure, less hemorrhage during opening and greater strength of restoration are possible with this technic as compared with other operative maneuvers in our hands. The opening in the bone which may be obtained is indicated in the roentgenogram in figure 8.

GENERAL COMMENT

It has been a matter of common experience, since Cushing [2] described the intermuscular subtemporal and the crossbow suboccipital decompressive operation, that cranial defects beneath the temporal and suboccipital muscles cause no special disability. The brain covered by muscle is

Fig. 7.—A specimen obtained at autopsy fifty-seven days after myoplastic suboccipital craniotomy. The bone is exposed above and muscle and the fascial diaphragm below. The anatomically perfect repair is evident. The bur hole openings were made at the time of the procedure so that the ventricles could be tapped to reduce the pressure. (The specimen was obtained through the courtesy of Dr. William Chase, Department of Pathology, Gill University.)

adequately protected from ordinary trauma, and the patients with such openings rarely complain of subjective symptoms.

The technic of Cushing has been accepted in practically all neurosurgical clinics on this continent and abroad without significant alteration. Healing of the wound has been good, and the plastic results have been satisfactory. In the temporal region, however, exposure is inade-

2. Cushing, H.: The Establishment of Cerebral Hernia as a Decompressive Measure for Inaccessible Brain Tumors; With the Description of Intermuscular Methods of Making the Bone Defect in the Temporal and Occipital Regions, Surg., Gynec. & Obst. **1**:297 (Oct.) 1905.

quate for anything but a simple decompression. With the muscle-splitting incision it is necessary to work beneath the covering of muscle, which often cannot be adequately retracted without tearing it from its attachment. In Cushing's occipital procedure the steps of exposure are time-consuming, and hemorrhage is troublesome. The fringe of muscle left attached to the nuchal ridge to permit of plastic repair interferes with exposure. Furthermore, closure is a laborious procedure.

We had followed Cushing's technic for subtemporal and suboccipital craniotomies habitually until two years ago, when we began to use the

Fig. 8.—A roentgenogram shows the opening in the bone in the patient shown in figure 4. The wide removal of bone and the removal of the posterior arch of the foramen magnum and the arch of the atlas are obvious.

myoplastic procedures we have described. Wider exposure has been possible. Healing of the wound has been unusually satisfactory. This is due to the fact that less dissection is required and there is less interference with the vascular supply of the flap since the relationship of the muscle to the scalp is not disturbed. Entirely satisfactory plastic repair has been obtained. The attachment of the muscles is so firm that even though intracranial pressure remains high no unsightly hernia can develop. The powerful muscles of the neck are as firmly attached as

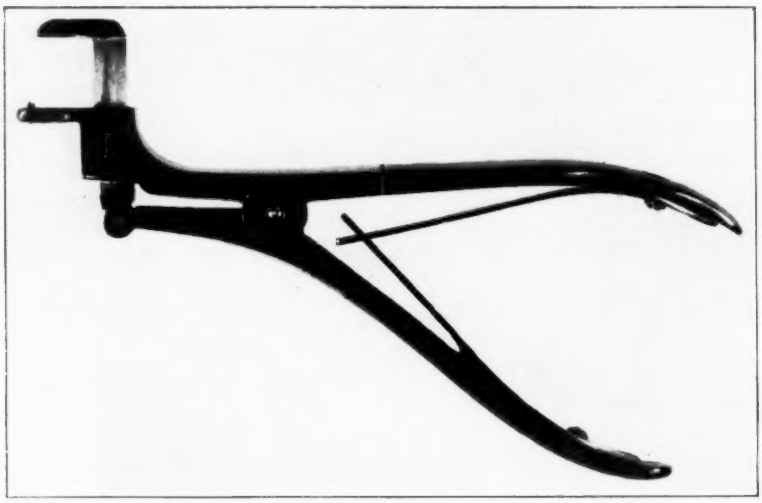

Fig. 9.—Barton's drill guide (made by Tiemann, 107 East Twenty-Eighth Street, New York).

Fig. 10.—The drill guide in use during closure of a suboccipital myoplastic craniotomy.

the temporal muscle fan. The facility of execution both in opening and in closing the wound has shortened the operative time considerably.

Dr. Lyman G. Barton of Plattsburg, N. Y., designed the useful instrument shown in figure 9. This drill guide makes it possible to cut very quickly the small holes through which the sutures to the muscle are passed. When the hole is being started the drill point is prevented from wandering by a slot in the upper foot. The drill point is stopped after passing through the skull by the under foot, with which it must come in contact. Figure 10 shows the instrument in use during the suboccipital procedure.

ABSTRACT OF DISCUSSION

Dr. Francis C. Grant, Philadelphia: When Dr. Cone spoke to me about this technic I was skeptical of its value, but I have seen some of his work in Montreal and had a chance to examine the pathologic specimen of which he showed the lantern slide. I was not sure that even when the muscle was united to the bone with wire the muscle and bone would form a firm union. However, according to the literature, it is possible physiologically for bone and muscle to form a perfect union. In the specimen that Dr. Cone showed, union followed the wires through into each of the holes.

The advantages of the method, particularly in the suboccipital craniotomy, are that the muscle is not incised, that troublesome hemorrhage may be avoided and that the bone is bitten off well up along the lateral sinus on the side on which the tumor lies. Previously, one has always been handicapped because of hesitation to take away too much of the bone, for in doing so the tag of muscle adherent to the bone to which one hoped to resuture the lower muscle flap might be damaged and prevent firm closure of the wound.

I think that with Dr. Cone's method one can assure oneself not only of better exposure, particularly above a tumor of the angle or above a lateral cerebellar tumor, but also of a closure which can be done more rapidly and with less bleeding. My opinion is that the technic is a distinct contribution to operative procedures in the posterior fossae.

Dr. W. James Gardner, Cleveland: My first reaction to the new procedures described by Dr. Cone and Dr. Penfield was rather similar to that of Dr. Grant. However, after reading the paper carefully and examining the illustrations, I was forced to the conclusion that the suboccipital procedure, at least, is very much worth while.

I should like to ask Dr. Cone whether the exposure by subtemporal craniotomy is sufficient to deal adequately with a fibroblastoma of the lesser wing of the sphenoid process. It seems to me that the closure of this subtemporal opening would be difficult if one found after preliminary exposure that the tumor extended well beyond the area where the temporal muscle is attached to the bone.

The suboccipital procedure permits a higher exposure, which is often of great advantage; it is particularly likely to be of advantage if during the removal of a tumor one of the subtemporal veins is injured. Unless one has quite a high bony opening, that accident may result in fatality on the operating table.

As to the method of tapping the ventricles, I differ with Dr. Cone, because I think that there are many advantages in tapping the ventricle through a separate incision placed above the main incision. If that is done and it should be advisable

to tap the ventricles postoperatively, it can be accomplished readily and with no discomfort to the patient.

Dr. Max Peet, Ann Arbor, Mich.: I have been using this technic for five or six years in operations requiring approach by way of the cerebellum. The procedure is the same as that outlined by Dr. Cone, except that he has made, I think, a valuable addition, that is, by drilling openings and suturing the muscle to the edge of the bone. Even without such suturing of the muscle to the bone, firm, satisfactory closure can be obtained. I have performed this operation without suturing the muscle to the bone with entire success in a large number of patients, both in bilateral cerebellar exposure and in a method of unilateral exposure which I have used for a number of years for the removal of tumor of the acoustic nerve.

I am certain that the new method of subtemporal decompression has advantages over the old method. I have not yet used it, but all those who have followed the old method realize how inadequate the removal of bone may be. This is because one is always afraid of separating the temporal muscle from its attachment. Now one can do so with impunity.

I can assure you, from extensive experience, that the suboccipital operation, in which sufficient bone is removed to expose at least the lower half of the lateral sinuses, is the procedure of choice for most operations on the cerebellum. It gives a much better view, especially of the upper part of the cerebellum, and the closure is more firm than that by any other method. Suturing the muscle layer to the bone, while not essential, assures a firm closure and is a worth while addition to the technic.

Dr. William Cone, Montreal, Canada: We worked out this technic after watching Dr. Peet. We felt that the exposures he obtained in operations on the posterior fossa were more satisfactory than those possible by the orthodox procedures for suboccipital craniotomy. Secure and safe restoration of the muscle to the bone was our chief concern. The simple technic we have described was evolved, and when it proved to be so satisfactory in suboccipital operations we used it in subtemporal craniotomies.

Dr. Gardner asked what can be done if the subtemporal exploration has been carried out by this method and a lesion is found which is too large to be satisfactorily handled through the exposure thus obtained. I think Dr. Gardner's comment that it would be difficult to convert this type of subtemporal exploration into a frontal, parietal or occipital one is valid. The method is not designed to supplant the osteoplastic type of operation, except perhaps in cases of a tumor or scar definitely limited to the temporal lobe.

EFFECTS OF LESIONS OF THE JUXTARESTIFORM BODY (I.A.K. BUNDLE) IN MACACUS RHESUS MONKEYS

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A frontal section through the medulla of the Macacus rhesus monkey at a level near the upper tip of the nucleus of Burdach reveals a small area situated dorsal to the remnant of the nucleus of Burdach and dorsomedial to the area ovalis of the restiform body. This area is well seen in preparations stained with Weigert's myelin sheath stain. Study with various methods, however, reveals that the area consists of a complex mixture of nerve cells and nerve fibers. Figure 1 shows this area near its caudal extremity, as demonstrated by the Weigert stain. In frontal sections more cephalad, the area increases in size and takes up a position medial and dorsomedial to the restiform body. In these more cephalad sections the cellular content of this area is seen to increase markedly. At a level near the entrance of the eighth nerve the area has become very large. Figure 2 shows this area near the entrance of the eighth nerve. It will be seen that on its dorsal and dorsomedial aspects it merges into the triangular and dorsal portions of the general vestibular nuclear complex. On its ventral border it is bounded by the spinal fifth root and nucleus and the reticular formation, into which it apparently sends some of its fibers. The position of this area remains relatively constant throughout its course to this level with respect to the restiform body. Many of the fibers of the entering eighth nerve pass into this complex structure. We shall consider the region we have just described as the intramedullary portion of the juxtarestiform body.

In more cephalad frontal sections, at levels where the inferior peduncle mass connecting the medulla with the cerebellum is formed, a second large bundle of fibers can be seen, which, however, differs from the first portion already described, in that the fibers are sectioned mainly longitudinally. This fiber bundle likewise has a position medial to the restiform body as the latter bends dorsally to enter the cerebellum.

From the Department of Neuropathology, New York State Psychiatric Institute and Hospital.

Read at the Sixty-First Annual Meeting of the American Neurological Association, Montreal, Canada, June 4, 1935.

Figure 3, a preparation from a Macacus rhesus monkey, stained by the Weigert method, reveals these fibers on frontal section as they run in a dorsomedial ventrolateral direction. We shall tentatively call this large mass of fibers the supramedullary portion of the juxtarestiform body, thus distinguishing it from the intramedullary portion already described. The supramedullary group of fibers, irrespective of the direction of the fibers, seems to be associated essentially with the more frontal dorsal portion of the vestibular nuclear complex and, as can be seen from

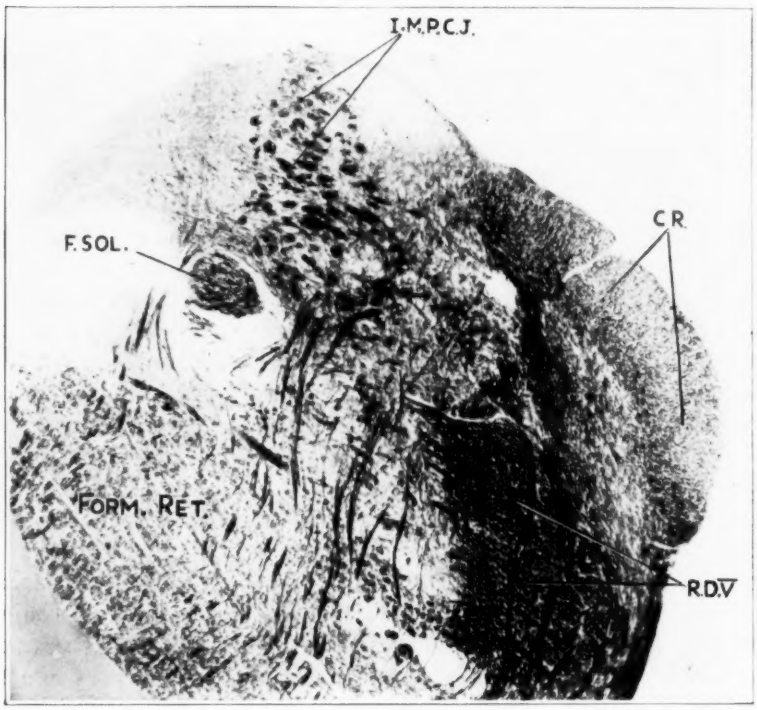

Fig. 1.—Frontal section of the medulla of a monkey near the most anterior tip of the nucleus of Burdach, showing the position of the fiber complex of the intramedullary portion of the juxtarestiform body. Weigert stain. *I-M.P.C.J.* indicates the intramedullary portion of the juxtarestiform body; *F.Sol.*, the fasciculus solitarius; *C.R.*, the restiform body; *R.D.V.*, the descending root of the fifth nerve, and *Form. Ret.*, the reticular formation.

figure 3, the fibers bend laterally around the wall of the fourth ventricle and appear to be connected mainly with the roof nuclear complex of the cerebellum. The majority of these fibers lie medial to the brachium conjunctivum, as this is formed at the hilus of the dentate nucleus. As most of both the intramedullary and the supramedullary portion just

described lie medial to the restiform body and its radiation into the cerebellum, they may be described as forming the juxtarestiform body.

These two relatively distinct systems of fibers have been variously described by many authors, and there has been a considerable difference of opinion concerning the exact fiber and cell content of each. In

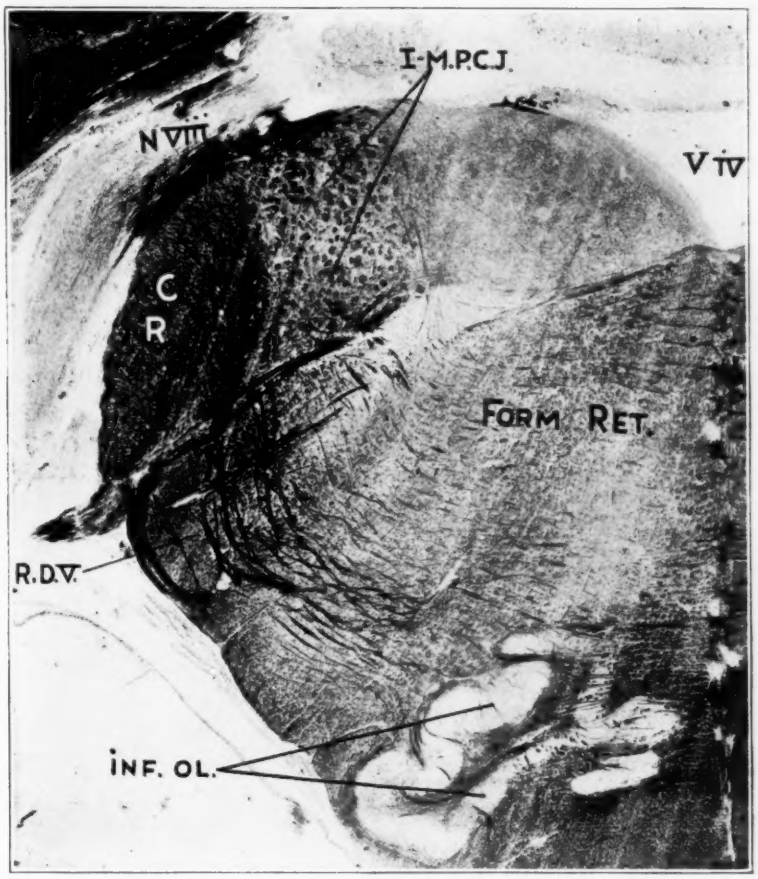

Fig. 2.—Frontal section of the medulla of a monkey near the zone of entrance of the eighth nerve, showing the well developed quadrilateral intramedullary portion of the juxtarestiform body. Weigert stain. *I-M.P.C.J.* indicates the intramedullary portion of the juxtarestiform body; *C.R.*, the restiform body; *R.D.V.*, the descending root of the fifth nerve; *Inf. Ol.*, the inferior olive; *N.VIII*, the eighth nerve; *V.iv.*, the fourth ventricle, and *Form.Ret.*, the reticular formation.

general, the tendency has been to consider the restiform body as the external portion of the inferior cerebellar peduncle and to consider the fiber and cell masses of both of the portions under discussion as

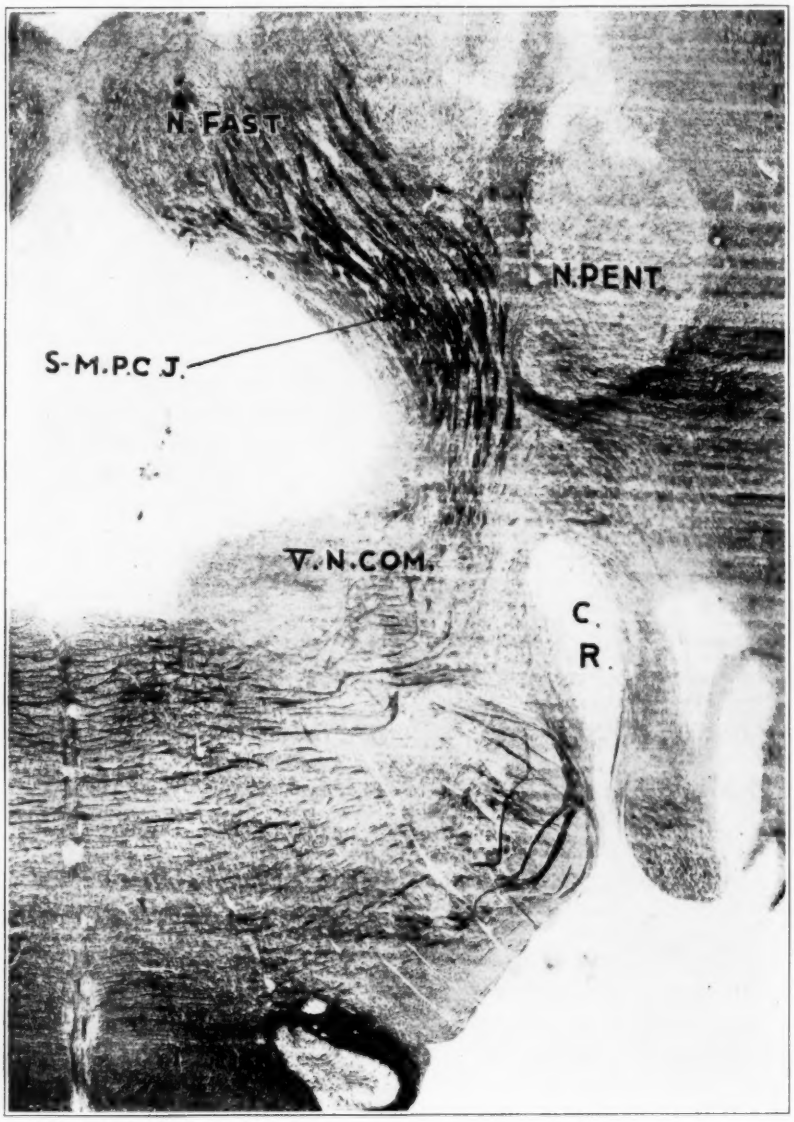

Fig. 3.—Frontal section of the medulla through the zone of entrance of the eighth nerve, showing the large group of fibers connecting the vestibular nuclear complex and the nuclei of the cerebellar roof, called the supramedullary portion of the juxtarestiform body. Weigert stain. *N.Fast.* indicates the nucleus fastigii; *S-M.P.C.J.*, the supramedullary portion of the juxtarestiform body; *V.N.Com.*, the vestibular nuclear complex, and *N.Dent.*, the dentate nucleus.

the inner portion of the inferior cerebellar peduncle. This apparently was meant when this region was called by Meynert [1] the *innere Abteilung des Kleinhirnstiels* (I.A.K.). This terminology has been accepted by Monakow,[2] Fuse [3] and others. Many writers consider this total region as the juxtarestiform body merely because of its topographic localization along the medial aspect of the restiform body. Some authors, among them Tilney and Riley,[4] have confined this term to the second system which we have delineated, namely, the supramedullary portion, and have considered the other system of fibers in the medulla and medial to the area ovalis as the lateral vestibular nucleus and descending vestibular root. These authors have usually held that the juxtarestiform body probably contains fibers relating the vestibular complex to the roof nuclei of the cerebellum. Finally, Winkler [5] apparently limited the term juxtarestiform body to the portion described by us as the intramedullary portion. No attempts have been made, so far as we are aware, to differentiate on a functional basis these two regions of the inner portion of the inferior cerebellar peduncle in the juxtarestiform body.

We cannot discuss at length here the probable differences in fiber and cell contents of these two regions, which we are studying in experimental anatomic preparations. We have attempted to place lesions so as to involve on the one hand the fibers connecting the vestibular nuclei with the roof nuclei of the cerebellum and on the other hand the lower intramedullary portion, so as to compare the effects of destruction of these two regions. To us, this seemed to be necessary if one would speak accurately of the function of the inferor cerebellar peduncle, especially since both of these regions are usually indiscriminately considered as forming the inner portion of the inferior cerebellar peduncle.

The symptoms following such lesions revealed, as we suspected, the presence of elements in these two systems which justify the separation of this general inner portion of the inferior cerebellar peduncle into at least two relatively independent systems. All lesions were controlled by serial frontal sections stained with the Weigert, Nissl or Marchi stain. In all, thirty-four monkeys were used for the study.

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1. Meynert, F., quoted by Fuse.[3]

2. Von Monakow, C.: Der rote Kern, die Haube und die Regio hypothalamica bei einigen Säugetieren und beim Menschen, Arb. a. d. hirnanat. Inst. in Zürich **4**:103, 1910; Striae acusticae und untere Schleife, Arch. f. Psychiat. **22**: 11, 1890.

3. Fuse, G.: Die innere Abteilung des Kleinhirnstiels (Meynert, I. A. K.) und der Deitersche Kern, Arb. a. d. hirnanat. Inst. in Zürich **4**:29, 1912.

4. Tilney, F., and Riley, H. A.: The Form and Functions of the Central Nervous System, ed. 2, New York, Paul B. Hoeber, Inc., 1923, p. 423.

5. Winkler, C.: Manuel de neurologie: L'anatomie du système nerveux, Haarlem, Netherlands, de Erven F. Bohn, 1921, vol. 1, pt. 1.

OPERATIVE TECHNIC

The cerebellum was exposed by a suboccipital approach, in which the occipital bones were removed well up over the transverse sinuses and as far laterally as was feasible. After reflection of the dura, the vermis and the lateral lobe of the cerebellum were carefully retracted upward, and by the use of small sponges and gentle suction the lateral wall of the ventricle could be clearly seen. The first type of lesion consisted of a superficial cut along the lateral wall of the ventricle at an angle of about 45 degrees to the horizontal. This was aimed at cutting the large bundle of fibers in the wall of the ventricle (supramedullary portion of the juxtarestiform body) at a point between the roof nuclei of the cerebellum and the vestibular nuclear masses. The other type of lesion, that involving the complex medial to the area ovalis (intramedullary portion), was produced by punching a longitudinal lesion in the dorsolateral surface of the medulla just medial to the dorsomedial tip of the area ovalis from a point approximating the most cephalic tip of the nucleus of Burdach and extending well up to the zone of entrance of the eighth nerve. The presence of complications was, of course, revealed by the serial anatomic study. We shall report here simply the observed behavioral changes in the monkey following lesions of these two types.

EFFECTS OF LESIONS

In general, the effects of the lesions may be divided into two groups:

1. *Section of the Supramedullary Portion of the Juxtarestiform Body.*—Figure 4 shows a lesion in a preparation stained by the Marchi method. This lesion, limited to the group of fibers in question, was associated nevertheless with the typical symptoms. Animals with unilateral section of these fibers presented fairly constant symptoms, including in the acute stage (twenty-four hours) nystagmus toward the side of the lesion, occasionally a slight twist of the chin toward the side of the lesion, slight staggering and occasional falling toward the opposite side, spiraling toward the opposite side on jumping and occasional slight ipsilateral hypotonia. No definite ataxia or other symptoms of cerebellar involvement were present in the pure cases. If the lesion was complicated, that is, if it extended deep enough to involve either the superior cerebellar peduncle or the restiform body radiation, ipsilateral symptoms of cerebellar involvement were present, which usually clouded the predominantly contralateral picture seen in the purer cases. If the lesion was placed too far ventrad symptoms of the type produced by lesions of the vestibular nuclei developed, which likewise clouded the picture seen in the pure cases. In the chronic stage, little that was abnormal remained in the pure cases. Most of the symptoms had disappeared by the end of ten days or two weeks. In the complicated cases, however, the symptoms, especially the ipsilateral symptoms, remained for a longer period.

In cases of bilateral lesions the symptoms were of essentially the same type if no complications were present, except that the nystagmus was predominantly upward and the falling on running and the spiraling on jumping were respectively backward and upward. A feature of these cases was the presence in the acute phase of a considerable degree of *Stutz* tonus, as manifested by a sharp extension of both front limbs when slight pressure was exerted from the shoulders on the plantar aspect of the feet. In the purer cases of bilateral lesions, as well as in the cases of unilateral lesions, the symptoms had practically disappeared by two weeks, after which the animal showed little that could be interpreted as abnormal.

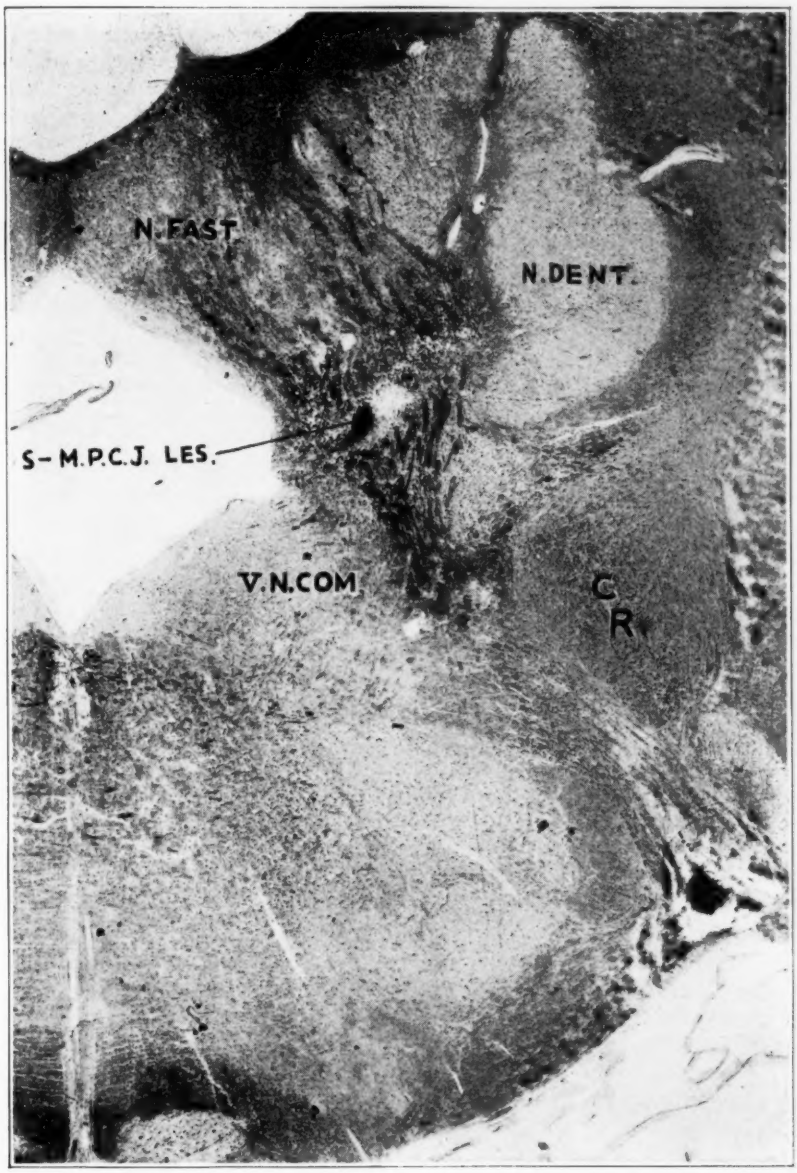

Fig. 4.—Frontal section through the zone of radiation of the supramedullary portion, showing a lesion, typical in distribution, sectioning the supramedullary portion nears its middle. Marchi stain. *N.Fast.* indicates nucleus fastigii; *N.Dent.*, the dentate nucleus; *S-M.P.C.J.*, lesion of the supramedullary portion of the juxta-restiform body; *V.N.Com.*, the vestibular nuclear complex, and *C.R.*, the restiform body.

2. *Lesions in the Intramedullary Portion of the Juxtarestiform Body (I. A. K.).*—When unilateral lesions were placed in this region the animals showed symptoms typical of extensive unilateral loss of the vestibular function of a central type. This occurred even when the lesion did not involve the trunk of the eighth nerve directly. In the acute phase an animal with such a unilateral lesion showed marked torsion of the head, with the chin toward the contralateral side and some flexion of the occiput toward the ipsilateral shoulder. There was in addition marked nystagmus toward the opposite side, with extension of the contralateral limbs and flexion of the ipsilateral limbs. In some cases, especially when the lesion involved even slightly the most dorsomedial tip of the restiform

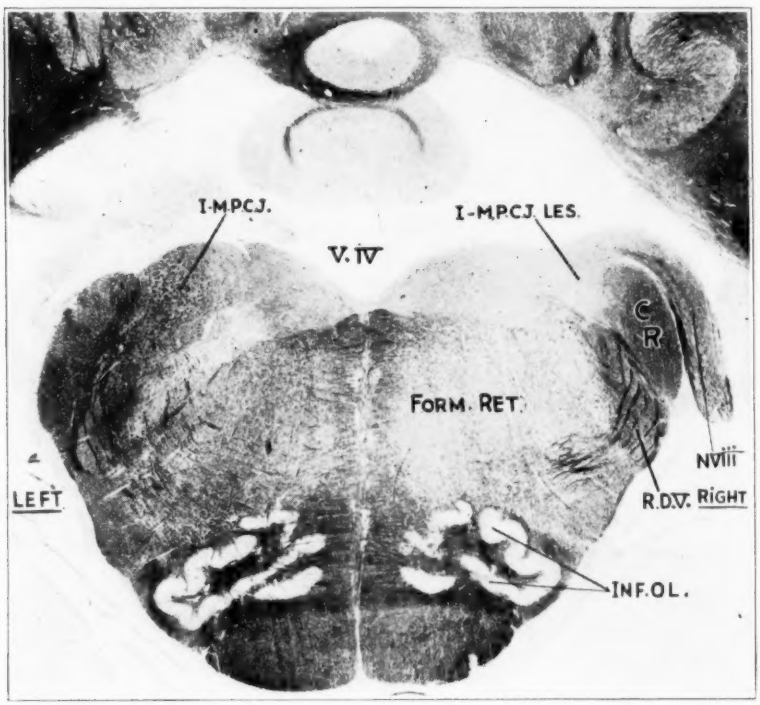

Fig. 5.—Frontal section of the medulla in a case in which a lesion had been produced several months previously involving the intramedullary portion of the juxtarestiform body on the right. The lesion involves very slightly the most dorsomedial tip of the restiform body. Weigert stain. *I-M.P.C.J.* indicates the intramedullary portion of the juxtarestiform body; *I-M.P.C.J. Les.*, the lesion of the intramedullary portion of the juxtarestiform body; *V.iv.*, the fourth ventricle; *N.VIII.*, the eigth nerve; *C.R.*, the restiform body; *Form. Ret.*, the reticular formation; *R.D.V.*, the descending root of the fifth nerve, and *Inf. Ol.*, the inferior olive.

body, there were marked rolling movements toward the side of the lesion. In general there were slight ipsilateral hypotonia and hyporeflexia. As far as could be determined, no gross sensory abnormality other than those of a vestibular origin were found. In general, the vestibular reflexes of the head on the side of

the lesion were absent. In the less severe cases, and in all cases after a short period of recovery which enabled the animal to walk, there were spiraling toward the side of the lesion on climbing or jumping and falling toward the side of the lesion in all movements of locomotion. Figure 5 shows a section of the medulla, stained by the Weigert method, which was taken from a monkey in which the lesion was unilateral. The whole area described as the intramedullary portion was completely destroyed, and, in addition, the scar of the lesion involved very slightly the most dorsomedial tip of the restiform body. The symptoms were of the forced type, marked rolling movements being manifested toward the side of the lesion. The animal was markedly disabled for approximately ten days, after which it recovered slowly but maintained, as did all other similar animals, a rather marked unilateral disability of the type produced by vestibular involvement even up to the time of being killed in the chronic stage after several months.

Up to the present we have not been able to produce exactly symmetrical lesions confined to the intramedullary portions of the juxtarestiform bodies on both sides. The lesions in all cases have been of different extent on the two sides or have involved some complicating features, such as associated lesions of the nucleus of Burdach or the restiform body on one or both sides. However, the general symptoms associated with such lesions and the impressions gained from a complete unilateral lesion, as presented in figure 5, lead us to the impression that complete bilateral lesions of the intramedullary portion of the juxtarestiform body would be associated with extremely severe and long lasting symptoms of vestibular involvement.

COMMENT

The results of lesions of the two portions of the juxtarestiform body, or I.A.K. bundle, which we have called the intramedullary and supramedullary portions, show definitely that it is unwise, at least from a physiologic point of view, to include both these portions under one common term. Even from the anatomic point of view considerable evidence has been brought forward to show that the regions under discussion are essentially different in content of fibers and cells. To be sure, they are both connected more or less directly with a common system, the vestibular system. One portion, however, the intramedullary portion, we consider to be essentially a region through which vestibular impulses are mediated to various portions of the medulla and the spinal cord. On the other hand, the supramedullary portion forms probably a system of fibers connecting the roof nuclei of the cerebellum and the vestibular nuclear complex in addition to direct fibers from the vestibular root to the roof nuclei. We have not attempted here to go into any detail concerning the exact anatomic relationships of these two regions. That there is some difference between the two regions can be seen on examination of a frontal section, such as is shown in figure 6, in which, despite the complete destruction of the intramedullary portion of the juxtarestiform body, the fibers of the supramedullary portion are relatively intact. It is conceivable that in this case a few fibers have disappeared from the supramedullary portion in question, but the majority of the fibers are preserved, indicating, we think, that the fibers

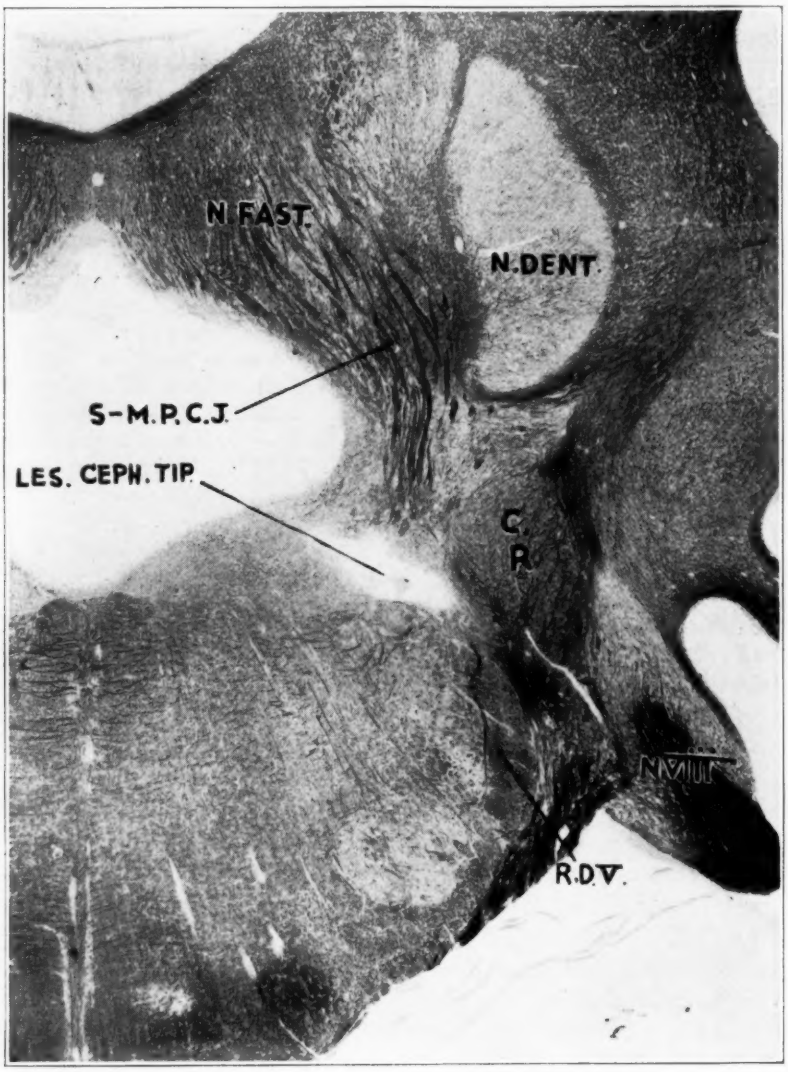

Fig. 6.—Frontal section through the zone of radiation of the supramedullary portion of the juxtarestiform body from the same case as figure 5. This section reveals good preservation of the supramedullary fibers despite complete destruction of the intramedullary portion of the juxtarestiform body. Weigert stain. *Les. Ceph. Tip.* indicates the lesion (cephalic tip); *S-M.P.C.J.*, the supramedullary portion of the juxtarestiform body; *N. Fast.*, the nucleus fastigii; *N. Dent.*, the dentate nucleus; *C.R.*, the restiform body; *R.D.V.*, the descending root of the fifth nerve, and *N.VIII.*, the eighth nerve.

in the supramedullary portion are associated with more cephalic and more dorsal portions of the vestibular nuclear complex. Similar anatomic deductions of a fairly gross character may be made in cases in which the supramedullary portion has been sectioned. In these cases preparations stained by the Marchi method at levels where the intra-

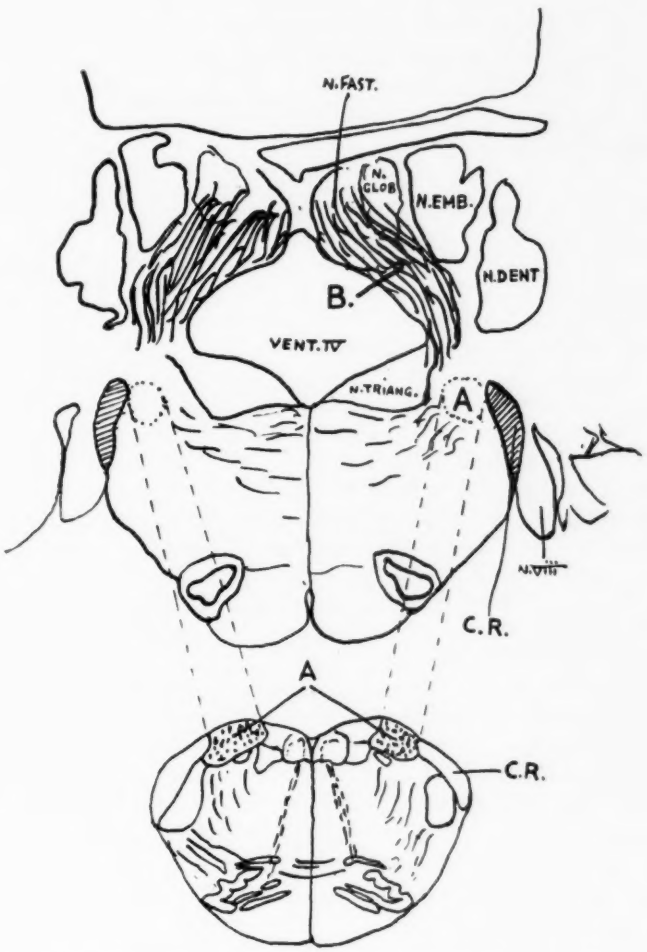

Fig. 7.—Diagram to indicate the general topography of the two regions under discussion. No attempt is made here to indicate any anatomic connections of these two regions. *A* indicates the intramedullary portion; *B.* the supramedullary portion and *C.R.*, the corpus restiforme.

medullary portion is well developed usually reveal only a slight degeneration within this intramedullary portion, thus indicating that possibly only a few fibers from the supramedullary portion pass into

the intramedullary portion. We think, therefore, that even a fairly gross anatomic study allows us to differentiate between the intramedullary and the supramedullary portion of the juxtarestiform body.

This anatomic evidence against a unification of all the elements in the juxtarestiform body under one term is further supported by the physiologic evidence resulting from lesions of the two portions. The effects of lesions of these two portions are so strikingly different that one seems justified in dividing the total complex into different physiologic as well as anatomic portions.

For final summary and orientation we may indicate the supramedullary portion of the juxtarestiform body by the letter B and the

TABLE 1.—*Symptoms Produced by a Lesion of Portion A (Intramedullary Portion)*

1. Falling—to side of lesion
2. Asymmetries in posture
(*a*) Head—chin to contralateral side
(*b*) Ipsilateral limbs flexed
(*c*) Contralateral limbs extended
3. Spontaneous nystagmus—to opposite side (quick component)
4. Ipsilateral hypotonia (slight)
5. Ipsilateral hyporeflexia (slight)
6. Rolling movements to side of lesion (inconstant)
7. Climbing—spiraling around long axis to same side
8. Jumping—spiraling around long axis to same side
9. Swimming—spiraling around long axis to same side
10. Absence of definite ataxia or dysmetria (perhaps clouded by severe symptoms of vestibular involvement)
11. Tendency of disabilities to be severe and long lasting

intramedullary portion by the letter A on a schematic diagram such as that presented in figure 7. In this diagram no attempt has been made to indicate any exact anatomic relationship of the parts under discussion. The scheme serves merely to indicate grossly the topography of these regions as they appear on frontal sections of the brain stem and as they are generally designated by workers investigating these portions of the nervous system.

Lesions of region A, as can be seen by reference to table 1, are associated with definite ipsilateral symptoms of a central type, indicating involvement of the vestibular mass, which is essentially the same type of symptoms that occur when the total vestibular mass of one side is destroyed, and it is no greater in degree even in cases in which lesions of portion A have extended sufficiently far to involve degeneration of portion B. This indicates that at least so far as the general vestibular

function of the body is concerned portion A is a very important if not the most important element of the vestibular nuclear complex.

TABLE 2.—*Symptoms Produced by a Lesion of Portion B (Supramedullary Portion)*

1. Falling—occasional, to side opposite the lesion
2. Asymmetries in posture
   (*a*) Head—usually normal but occasionally shows slight twist of chin toward ipsilateral side
   (*b*) } Body and limb posture normal
   (*c*) }
3. Spontaneous nystagmus—to side of lesion
4. Ipsilateral hypotonia (slight and inconstant)
5. Ipsilateral hyporeflexia (slight and inconstant)
6. Absence of rolling movements
7. Climbing—spiraling around long axis to opposite side
8. Jumping—spiraling around long axis to opposite side
9. Swimming—essentially normal
10. Absence of definite ataxia or dysmetria in purest cases
11. Relative slight degree of disabilities as compared to those following lesions of A; tendency to disappear rather rapidly

TABLE 3.—*Symptoms Produced by Section of the Corpus Restiforme Plus a Lesion of Portion A (Lesion of the Total Inferior Peduncle—Inner and Outer Portions)*

1. Falling—to side of lesion
2. Asymmetries in posture
   (*a*) Head—chin to contralateral side
   (*b*) Ipsilateral limbs flexed
   (*c*) Contralateral limbs extended
3. Spontaneous nystagmus to opposite side
4. Ipsilateral hypotonia (moderate)
5. Ipsilateral hyporeflexia (moderate)
6. Rolling movements to side of lesion
7. Climbing—spiraling around long axis to same side
8. Jumping—spiraling around long axis to same side
9. Swimming—spiraling around long axis to same side
10. Ataxia and dysmetria—(clouded in acute stage by severe symptoms of vestibular involvement)
11. Relatively severe degree of disabilities; tendency to be long lasting; the predominance of vestibular elements

Section of portion B, as indicated by table 2, as associated with symptoms which in our experience are, though mild, essentially of the type seen in cases of vestibular involvement, including occasional slight torsion of the head, nystagmus, spiraling on jumping and slight hypotonia.

With the exception of the hypotonia, symptoms of this type have been found by us only in cases of lesions in which structures connected with the vestibular mechanism have in some way been involved. The interesting feature regarding these symptoms subsequent to section of region B is that in this case the symptoms are contralateral to the side of the lesion, whereas usually in a case of simple vestibular involvement the symptoms are ipsilateral. We cannot say at present to just what this contralaterality of the symptoms is due. In addition, the symptoms, while probably of vestibular origin, are very mild when compared with those associated with lesions of the vestibular nuclei. In general, then, lesions of the intramedullary portion of the juxtarestiform body are associated with severe typical ipsilateral symptoms of vestibular involvement, whereas those of the supramedullary portion are associated with

TABLE 4.—*Symptoms Produced by Section of the Corpus Restiforme*

1. Falling—inconstant to side of lesion
2. Absence of asymmetries in posture
3. No spontaneous nystagmus
4. Ipsilateral hypotonia (moderate)
5. Ipsilateral hyporeflexia (moderate)
6. Absence of rolling movements
7. Absence of spiraling in climbing
8. Absence of spiraling in jumping
9. Normal swimming
10. Ipsilateral ataxia and dysmetria
11. Relatively slight degree of disabilities; tendency to disappear apparently practically completely

symptoms which we believe likewise include some vestibular elements but which are much milder and contralateral.

An examination of the symptoms produced by lesions of parts B and A of the juxtarestiform body reveals how confusing it is to include both parts B and A in the term juxtarestiform body, or I.A.K., especially when this term is used to signify the inner portion of the inferior cerebellar peduncle. If one does this and then proceeds to cut the total inferior cerebellar peduncle in the monkey, especially at a point below the entrance of the eighth nerve so as to involve in addition to the restiform body the part A of our experiment, one finds that the symptoms resulting from section of the inferior cerebellar peduncle are predominantly of the type seen in cases of vestibular involvement. Table 3 indicates that this is the case. This brings up the seemingly paradoxical consideration that the function of the inferior cerebellar peduncle is predominantly vestibular. The truth is that when one sections the external portion, or the restiform body, one finds, as

previously reported by us,[6] and as table 4 indicates, that the symptoms are essentially not those of vestibular involvement, whereas if one makes a lesion of the inner portion, especially in portion A, the symptoms are predominantly those of vestibular involvement.

Part A is undoubtedly a major portion of the central vestibular mechanism and should more accurately be considered as such. Portion B, though presumably a fiber system relating the older roof nuclear mass of the cerebellum and some of the central vestibular nuclear mass, should also be considered in final analysis as independent of the inferior cerebellar peduncle.

SUMMARY

Two types of lesions were produced in thirty-four Macacus rhesus monkeys. In one type, the large periventricular fiber mass, apparently connecting the roof nuclei of the cerebellum with the vestibular nuclear mass, was sectioned on one side or on both sides. The fiber mass thus sectioned we have called the supramedullary portion of the juxtarestiform body. The other type of lesion involved the fiber and cell complex cephalad to the dorsal column nuclei and medial to the dorsomedial portion of the restiform body. This area we have called the intramedullary portion of the juxtarestiform body, or the I.A.K. system.

The effects of lesions of the supramedullary and intramedullary portions of the juxtarestiform body were different. Lesions of one intramedullary portion produced ipsilateral symptoms of the type seen in cases of vestibular involvement, including torsion of the chin toward the opposite side, flexion of the occiput on the ipsilateral shoulder, contralateral extension and ipsilateral flexion of the limbs, ipsilateral hypotonia and hyporeflexia, spiraling toward the same side on jumping and climbing, nystagmus toward the contralateral side, and falling with rolling movements toward the side of the lesion in some cases. Unilateral lesions of the supramedullary portion were associated with nystagmus toward the side of the lesion, falling toward the opposite side, spiraling toward the side opposite the lesion on jumping and climbing and slight ipsilateral hypotonia.

Bilateral lesions of the intramedullary portions were associated with bilateral severe symptoms of vestibular involvement. Bilateral lesions of the supramedullary portions were associated with rather definite *Stutz* tonus in the acute phase. In addition, the nystagmus was predominantly upward and there was some apparent disorientation in space on quick movements. This, we think, was manifested principally in jumping, when the animal usually turned back flips.

6. Ferraro, A., and Barrera, S. E.: The Effects of Lesions of the Dorsal Spino-Cerebellar Tract and Corpus Restiforme in the Macacus Rhesus Monkey, Brain **58**:174 (June) 1935.

The differences between the symptom pictures following lesions of the intramedullary and supramedullary portions of the juxtarestiform body failed to justify the inclusion of both these portions under a single term and justified the separation of the two portions, at least on a physiologic basis.

If both regions are included uncritically in the inner portion of the inferior cerebellar peduncle it will be found on experiment that complete section of the inferior cerebellar peduncle is associated with a symptom complex which is predominantly of the type produced by vestibular involvement. This does not appear satisfactory when one portion, the inner portion, can be denominated and proved to be predominantly vestibular in function, whereas the outer portion formed by the restiform body proper can be shown to be essentially cerebellar in function.

DISCUSSION

Dr. Adolph Meyer, Baltimore: This presentation brings up remembrances of a ghost, that is to say, the cultivation of one of those fates of brain anatomy and neurology which, unfortunately, in the hands of von Monakow and quite a number of other men was used for visions of complexity rather than of definition. I was surprised to hear the region mentioned in these old terms in relation to the restiform body. To mention it as juxtarestiform seems to me to be bewildering and, as I say, reminiscent of a time when the knowledge concerning the vestibular nerve was not as clear as it is now.

I wish to ask to what extent this area has been studied in specimens in which the vestibular nerve had been previously eliminated. One is dealing here essentially with a problem involving the vestibular apparatus and with the structures among which the vestibular apparatus terminates. Evidently one part of the vestibular nerve goes to the inner arm of the cerebellum and another part goes to that very vital part of the brain axis which divides that solid unit called the head and that freely movable part, the neck—a juncture which is largely regulated by vestibular function. The question then will be: Have these studies also been made on animals prepared by elimination of the vestibular nerve by previous operation and degeneration? If so, one could approach the question of whether in that field of termination it has been possible to find any of the complications that are found in the descriptions that came from the laboratory of von Monakow. Of course, one is touching here fields in which friendships, interests and allegiances may be involved; but it ought not to be an encroachment on one's admiration for those men who have used a traditional terminology and appeals to complexity. I should certainly like to see the region under discussion definitely connected with the vestibular, as a vestibular termination field, and the question settled whether there are any of those great complications that were held before one when one studied the anatomy of the brain before the investigators were wise enough to use preparatory operations and to get away from purely topographic propinquities.

Dr. Leslie B. Hohman, Baltimore: I should like to ask whether bilateral lesions were made in the pathways going from the vestibular nucleus to the roof nuclei, since there are crossed pathways.

Dr. S. E. Barrera, New York: In answer to Dr. Meyer, I may say that we respect immensely the original anatomic descriptions in this field, such as those of

von Monakow and others. It was our point to emphasize precisely the essentially vestibular nature of the juxtarestiform body in relation to the cerebellum, in which we are particularly interested at present. We did not consider it wise to correlate functionally this large area in the medulla to the restiform body. In the nomenclature, however, we used merely terminology such, for example, as Winkler uses in his textbook on neuro-anatomy, in which he designates this large area dorsomedial to the restiform body as the I.A.K. or the corpus juxtarestiforme. The scope of our investigation was to establish whether this area should be considered functionally as a part of the restiform system. We have reached the conclusion that it should not be considered as a part of the restiform body but as a part of the vestibular system. We are at present making anatomic studies of the whole region and hope to be able to throw some light on its anatomic connections.

Two experiments, however, may throw some light on the other question which Dr. Meyer asked. In one animal we performed bilateral labyrinthectomy. Subsequently, both nerves were found on serial section to be degenerated. At a second operation a large vestibular nuclear lesion was made on one side, following which there developed typical unilateral, ipsilateral vestibular symptoms, which indicates to some extent the complexity of this region, since typical unilateral vestibular symptoms could occur even in the absence of both vestibular peripheral receptors.

In another case we produced bilateral lesions of portion B, or the bundle of fibers running from the nuclei to the cerebellar nuclear roof; three months after this we performed unilateral labyrinthectomy; much to our surprise none of the asymmetrical symptoms associated with unilateral section of the eighth nerve or labyrinthectomy occurred in this case. However, this is under further investigation.

We have produced bilateral lesions of portion B. It is interesting that in these cases the asymmetries in the sense of torsion or locomotion were upward and backward, that is, when the animal attempted to jump, instead of spiraling toward the side of the lesion it spiraled upward and backward, turning back flips. There was a tendency toward dorsiflexion of the head, and the nystagmus was in the vertical plane, usually upward. In these cases, also, there was a definite *Stutztonus* in the sense of Rademacher. With the slightest pressure on the soles of the feet or downward on the shoulders the animal presented marked rigidity of the front limbs.

HYPERTHERMIA DUE TO LESIONS IN THE HYPOTHALAMUS

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There is good evidence that the hypothalamus is an important area for the maintenance of normal body temperature and that it contains probably important nerve centers concerned with the regulation of temperature. The importance of this region in general for this particular function was shown by the experiments of Isenschmid and Krehl,[1] who found that when the brain stem of rabbits was divided at the junction of the diencephalon and the mesencephalon, all power of temperature control was lost. On the other hand, they found that when the cerebrum and the corpus striatum were removed, no loss of temperature regulation resulted. These observations were carried further by Isenschmid and Schnitzler,[2] who found that the tuber cinereum was the most important part of the brain for the regulation of temperature. They observed that an injury at the junction of the diencephalon and the mesencephalon caused a disturbance of temperature control.

The importance of the hypothalamus in the regulation of temperature was clearly demonstrated by the experiments of Keller and Hare,[3] who found that hypothalamic animals could regulate heat, while midbrain animals could not. Unilateral removal of the hypothalamus did not disturb the regulation of heat. A bilateral lesion in the same region impaired the power of the animal to maintain body temperature. When the whole hypothalamus was cut away, the ability to maintain body temperature was entirely lost, and shivering could not be elicited. "These observations indicate that the chief central mechanism controlling heat production is located in the hypothalamus, and that extirpation of this region releases the heat loss mechanism, located elsewhere, from coordinated control."

From the Laboratory of Neurosurgery of the University of Pennsylvania Hospital.

Read at the Sixty-First Annual Meeting of the American Neurological Association, Montreal, Canada, June 3, 1935.

1. Isenschmid, v. R., and Krehl, L.: Ueber den Einfluss des Gehirns auf die Wärmeregulation, Arch. f. exper. Path. u. Pharmakol. **70**:109, 1912.

2. Isenschmid, v. R., and Schnitzler, W.: Beitrag zur Lokalisation des Wärmeregulation vorstehenden Zentralapparates im Zwischenhirn, Arch. f. exper. Path. u. Pharmakol. **76**:202, 1914.

3. Keller, A. O., and Hare, W. K.: The Hypothalamus and Heat Regulation, Proc. Soc. Exper. Biol. & Med. **29**:1069 (June) 1932.

A more precise localization of the temperature-regulating centers in the hypothalamus was afforded by the work of Bazett, Alpers and Erb,[4] who found that the infundibular nuclei (Winkler) or the anterior hypothalamic nuclei (Rioch) were the most important areas concerned in the regulation of temperature in the cat. These areas correspond to the substantia grisea of the third ventricle (Malone) in man. The hypothalamus was studied in serial section in these animals. The thalamus was found not to be important in the regulation of temperature in cats.

There appears to be little question, therefore, that the hypothalamus is a very important area in the function of temperature control. That it is not the only "center," however, is equally certain, for the work of others attests that both the higher and the lower areas in the brain perform some function in the regulation of temperature. Attention has been called many times to the importance of the area of the corpus striatum (Aronsohn and Sachs,[5] Barbour[6] and Hashimoto[7]). More recently, Pinkston, Bard and Rioch[8] indicated clearly that the cortical level also is important in the normal control of temperature. Cats and dogs from which the neopallium had been removed showed distinct changes, such as chronic vasodilatation with failure of the vessels of the skin to react normally to cold, absence of true polypneic panting, delayed hyperpnea, a rise in rectal temperature before hyperpnea developed and immediate and vigorous shivering in response to cold, with often a rise in body temperature, in contrast to delayed shivering before operation and a fall of body temperature. These same animals with the cortex removed and the hypothalamus intact were able to maintain normal body temperature. There seems to be a distinct disturbance in the heat loss mechanism in decorticated cats and dogs, with retention of the ability to regulate bodily temperature, however, so long as the hypothalamus is intact.

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4. Bazett, H. C.; Alpers, B. J., and Erb, W. H.: Hypothalamus and Temperature Control, Arch. Neurol. & Psychiat. **30**:728 (Oct.) 1933.

5. Aronsohn, E., and Sachs, J.: Die Beziehungen des Gehirns zur Körperwärme und zum Fieber, Arch. f. d. ges. Physiol. **33**:232, 1885.

6. Barbour, H. G.: Die Wirkung unmittelbarer Erwärmung und Abkühlung der Wärmezentra auf die Körpertemperatur, Arch. f. exper. Path. u. Pharmakol. **70**:1, 1912.

7. Hashimoto, M.: Ueber den Einfluss unmittelbarer Erwärmung und Abkühlung des Wärmezentrums auf die Temperaturwirkungen von verschiedenen pyrogenen und antipyretischen Substanzen, Arch. f. exper. Path. u. Pharmakol. **78**:394, 1915.

8. Pinkston, J. O.; Bard, P., and Rioch, D. McK.: The Responses to Changes in Environmental Temperature After Removal of Portions of the Forebrain, Am. J. Physiol. **109**:515 (Sept.) 1934.

Further evidence that other levels in addition to the hypothalamus are concerned in the control of temperature is illustrated clearly by the work of Keller (1933), who maintained that heat-conducting pathways mediating heat regulation pass caudally through the midbrain and the pons. Furthermore, he found that medullary cats have hyperthermia and the ability to shiver, indicating that there may be a subsidiary center in the medulla for the regulation of heat.

The nervous mechanism of heat regulation, therefore, seems to stretch from the cortex to the medulla, implicating the striatum, hypothalamus, midbrain pons and medulla, either by "centers" or by pathways. In this mechanism the hypothalamic region seems to come closest to acting as a center. Certainly it is the most important part of the mechanism. To say, however, that this is so indicates only in a general way the function of the hypothalamic region in the regulation of temperature. It is essential to know exactly what parts of the hypothalamus are important for regulation and how this regulation is effected. Bazett, Alpers and Erb have demonstrated that the region of the infundibular nuclei (Winkler) or the anterior hypothalamic nuclei (Rioch) is important in cats. Further study of this area is essential. Serial sections of the hypothalamus were studied in two cases of suprasellar cyst in patients who died with hyperthermia in order to determine what areas are injured in man in this type of disorder of temperature regulation.

REPORT OF CASES

The report of the cases will be brief because the only really essential aspect of them is the terminal hyperthermia from which both patients suffered.

CASE 1.—*Signs of an intrasellar tumor. Operative disclosure of a large suprasellar cyst, removed in toto. Death with hyperthermia in twenty-four hours.*

History.—E. H., a woman aged 54, entered the Graduate Hospital of the University of Pennsylvania on April 24, 1934, in the care of Dr. F. C. Grant. She complained of pain and failing vision in both eyes. In February 1934 she had pain over the anterior abdominal wall and a severe cold in the head. Pus drained profusely from her nose, and when this ceased she had severe headache over the whole head. In a short time vision in the right eye became blurred, followed soon by impairment of vision in the left eye. At the same time there developed severe frontal headache.

Examination.—There were bilateral primary atrophy of the optic nerve, bitemporal hemianopia and some disturbances suggesting involvement of the endocrine system, such as coarse dry skin, obesity and features suggestive of acromegaly. Examination of the skull revealed the deformity typical of an intrasellar tumor. The pituitary fossa was markedly enlarged, the measurements being 24 by 22 mm. There was marked encroachment on the sphenoid sinus. The basal metabolic rate was 23. The spinal fluid pressure was 265 mm. of water. Serologic tests of the blood and spinal fluid gave negative results. Other routine tests of the blood gave negative results.

Operation.—On May 3 Dr. F. C. Grant performed a right transfrontal craniotomy and exposed the sella turcica by the intradural approach. The tumor was seen presenting behind the right optic nerve; a small piece was removed for study. There was no undue pressure on the base of the brain and no excessive bleeding throughout the operation. The patient left the operating table in good condition.

Course.—The patient did not rally from the operation. The temperature had ranged from 97.6 to 98.8 F. for nine days. On the day preceding operation it fell to 96.8 F. and rose slowly during twenty-four hours to 99 F. (rectally). Immediately after operation it began to rise, going to 101.8 F., falling to 101.2 F. and then rising gradually in the course of seven hours to 102.8 F. There then

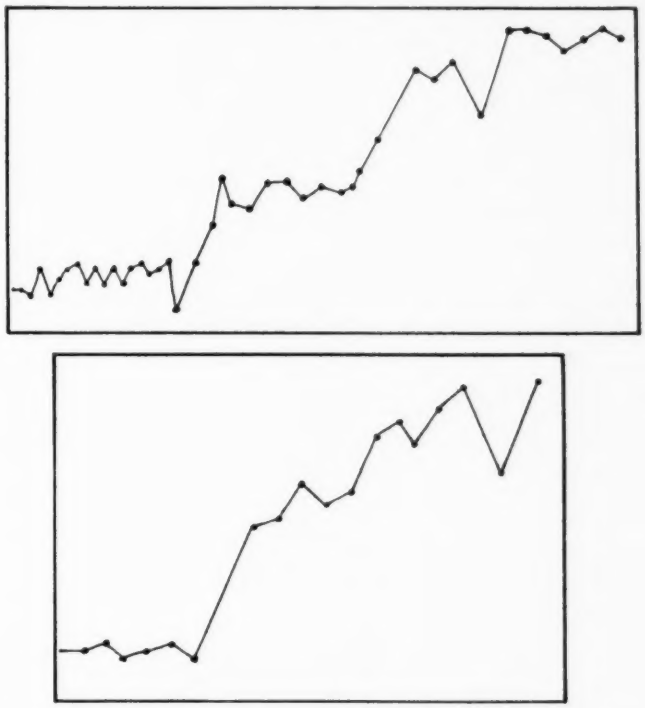

Fig. 1.—Temperature charts of the two patients. In the upper chart (case 1) the terminal temperature is about 107 F., and in the lower one (case 2), 106.2 F.

followed a very sudden rise to 105.8 F., followed by a brief fall to 104 F., then another steep rise to 107.2 F. and finally death with a temperature of 106.8 F.

Necropsy.—The operative field was perfectly dry. At the base of the brain was a large tumor in the region of the pituitary gland. It filled the entire space between the hippocampal gyri, extending from the optic chiasm to the anterior border of the pons. The growth was removed without tearing the base of the brain. In the bed one could make out compression and flattening of the optic nerves, optic chiasm and floor of the diencephalon. The right optic nerve in particular was flattened. The optic chiasm was so compressed that it could not be made out. A thin film of hemorrhage covered the entire floor of the brain in this region.

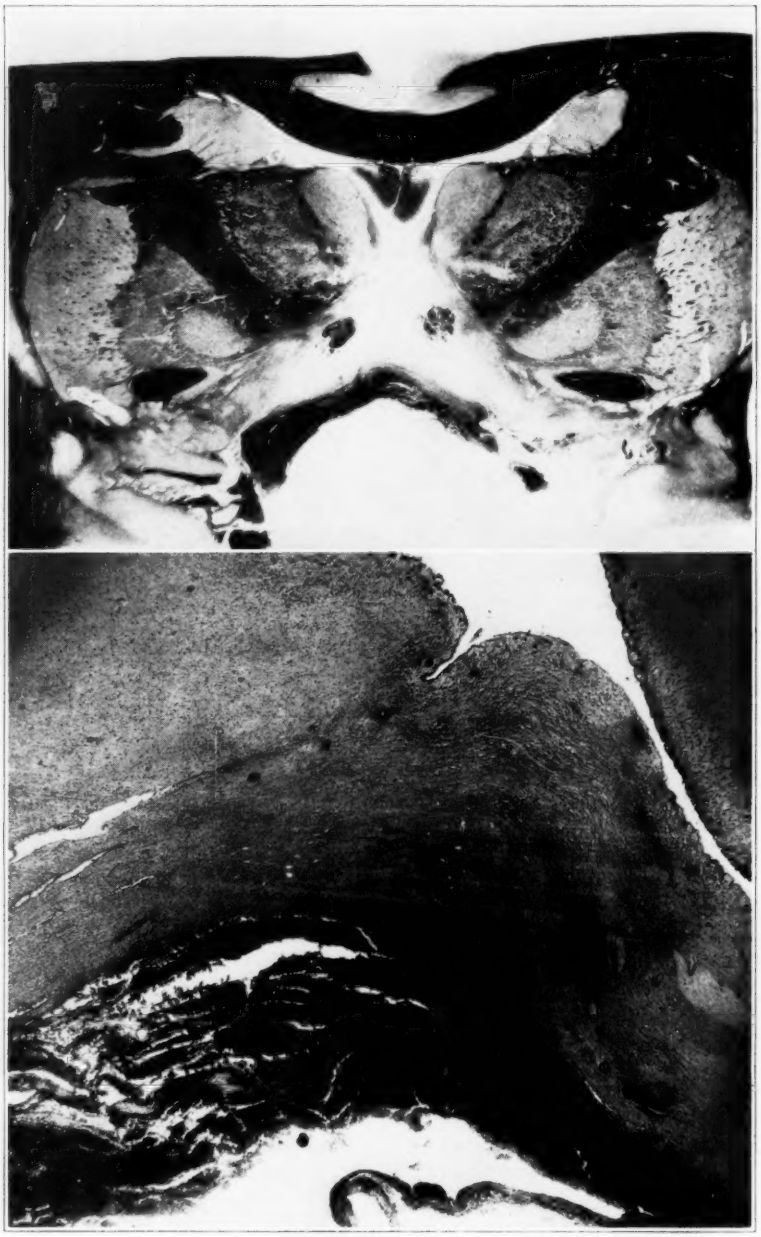

Fig. 2 (case 1).—The upper photograph shows the marked distortion of the hypothalamus by the wall of the cyst. The section is stained with the myelin sheath stain. The lower photograph shows the area of destruction in the hypothalamus, particularly the substantia grisea in the floor of the third ventricle. There is slight destruction of the hypothalamic area somewhat lateral to this region. The section is stained by the Van Gieson method.

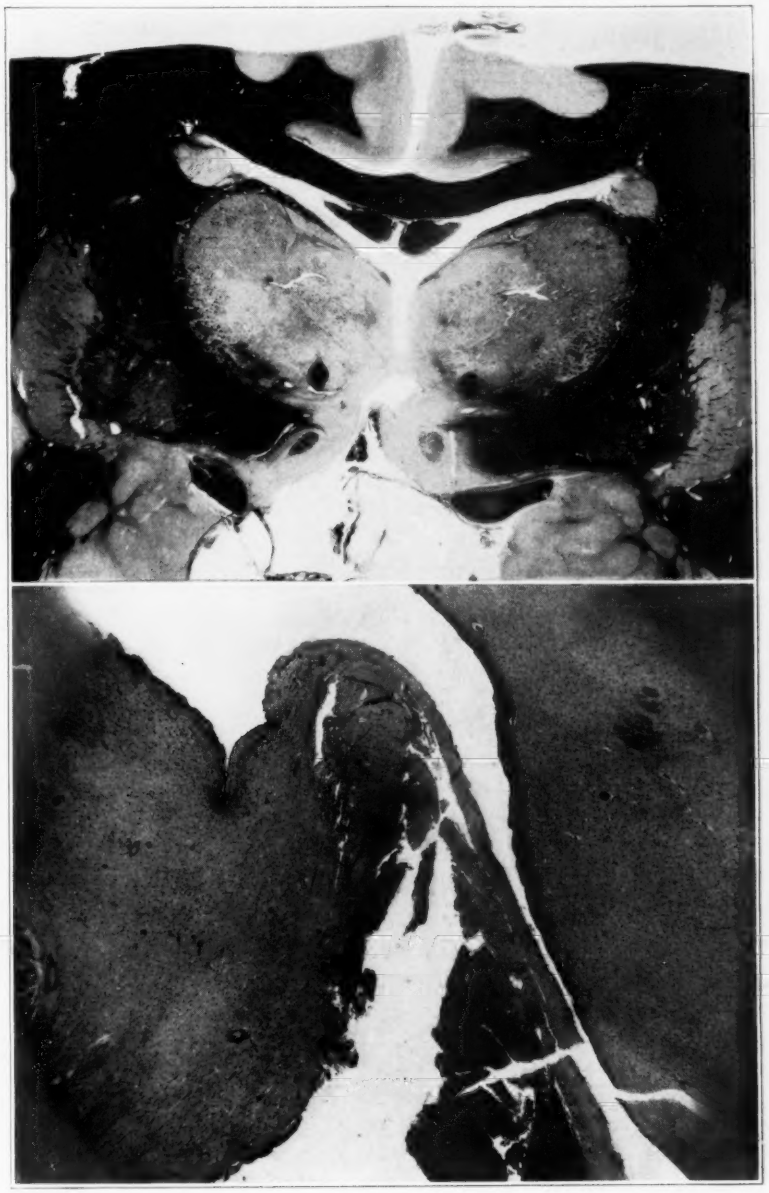

Fig. 3 (case 1).—A more posterior view of the hypothalamus, showing the destruction of the substantia grisea in the floor of the third ventricle and the more pronounced disintegration of the tissue slightly lateral to this. The fornix is seen in the extreme lateral portion of the field on the left side.

CASE 2.—*Pain over the right eye. Blurring vision. Paracentral scotomas in both temporal fields, progressing to bitemporal hemianopia and later loss of vision in the left eye. Removal of a suprasellar cyst. Vasomotor collapse and death with hyperthermia in twenty-four hours.*

History.—S. H., a Jewish man aged 29, entered the Mount Sinai Hospital in the care of Dr. A. Barlow. He had been well until three years previously, when he suffered with acute sinusitis, which was followed by attacks of severe pain over the right eye. About five weeks before entrance pain developed deep in the right eye. This was followed by blurring of vision, especially in the right eye, five days before entrance into hospital; it was this which brought him to the hospital for treatment.

Examination.—Nothing abnormal was detected in the general systemic review. The important findings were limited to the eyes. The optic disks when first examined were normal in color, but there was a bitemporal paracentral scotoma. Vision was markedly reduced in each eye, being 10/200 in the right eye and 20/40 in the left. There was bitemporal hemianopia for color but not for form. During the next two weeks the patient became completely blind. The paracentral scotomas expanded in each field until there developed bitemporal hemianopia for form. This continued to develop in the left eye to complete loss of the visual field, while the temporal hemianopia remained in the right field. There were no other significant neurologic findings and no signs suggesting disturbances of the endocrine system. A roentgenogram of the skull revealed an enlarged sella turcica, measuring 16 mm. long. Examination of the blood and spinal fluid gave negative results in all details.

Operation.—On April 14 Dr. Francis C. Grant reflected a bone flap in the right frontal region and exposed a cystic tumor arising from the pituitary fossa beneath the chiasm. Its walls were so thin that it looked like an arachnoid cyst, and clear fluid was removed from it. By gentle traction the wall of the cyst was completely removed without apparent trauma to the brain.

Course.—The patient left the operating room in fair condition. Within six hours he had an axillary temperature of 104 F., and the blood pressure could not be measured. The temperature continued to rise, despite transfusions, and he died within twenty-four hours with a temperature of 106 F.

Necropsy.—There was marked distortion of the base of the brain with a deep excavation in the region of the floor of the diencephalon. The entire tumor mass seemed to be removed, but there remained a thickened membrane which was attached to the chiasm and the floor of the third ventricle. Otherwise gross examination of the brain gave negative results.

Histologic Studies.—Serial sections were made of the entire hypothalamus in both cases. Alternate sections were studied with Weil's stain and Van Gieson's method. Every fourth section was stained and studied.

CASE 1.—The entire floor of the diencephalon was distorted by the pressure of the tumor. The structures were pushed up and somewhat laterally, but they could still be identified readily.

Cell studies revealed that the entire floor of the third ventricle was destroyed. In some parts it was actually gone, so that the third ventricle was in direct communication with the arachnoid space. It looked as if it had been pulled away during the course of manipulation. The destroyed area corresponded to the substantia grisea of the third ventricle of Malone. The gray matter in the floor of the third ventricle was completely destroyed throughout the extent of the

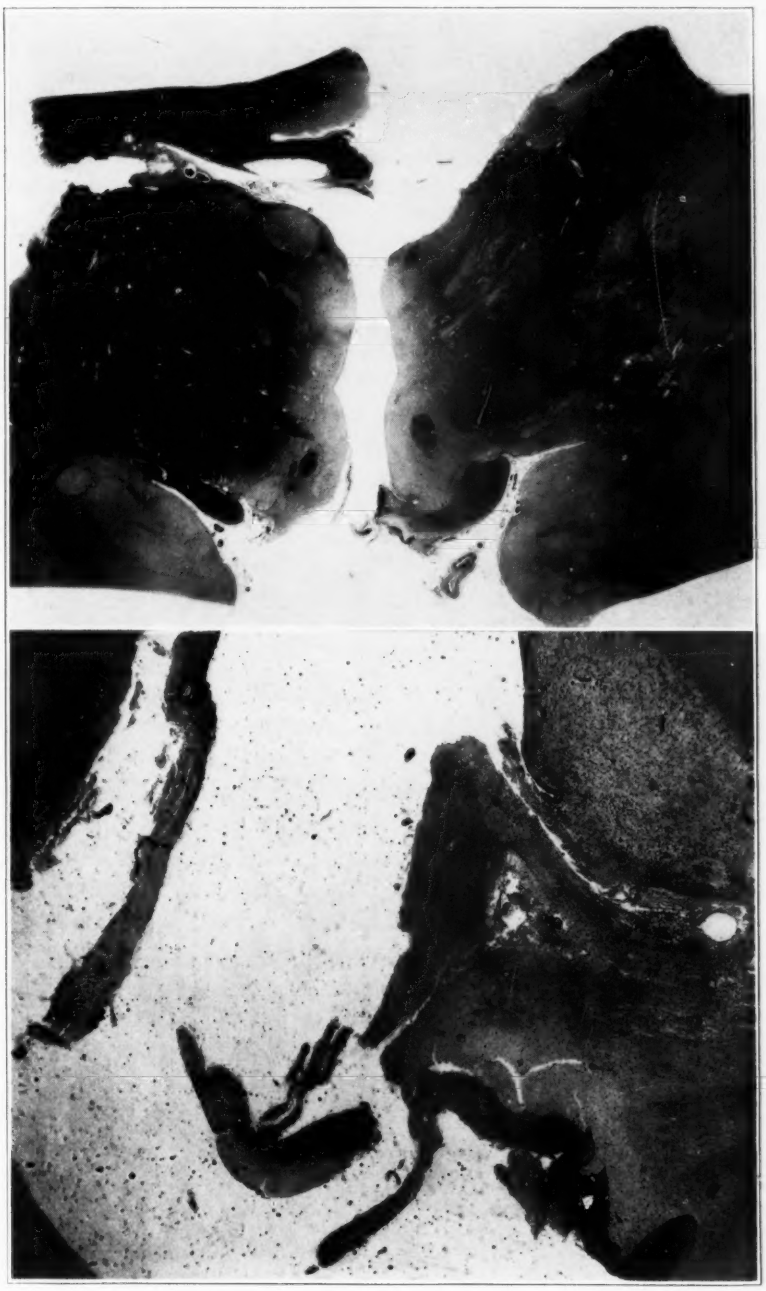

Fig. 4 (case 2).—The photographs show destruction of the floor of the third ventricle, more particularly in the section in the lower photograph, stained by the Van Gieson method. Complete disruption of the substantia grisea, and to a lesser extent of the fields just lateral to it, is shown.

diencephalon. This destruction was due to actual tearing away of the structures or to hemorrhage and softening in the implicated regions. The destruction extended somewhat laterally over the floor of the tuber cinereum, destroying some of the tissue lying lateral to the substantia grisea but not extending very far laterally or deeply. The small nerve cells of the substantia grisea were almost completely destroyed; very few remained, and these were definitely diseased. In addition, there was destruction of isolated portions of the nucleus tuberomamillaris, but by far the greater bulk of the nuclear mass was preserved. Small areas of the medial parts of this nucleus close to the wall of the third ventricle were destroyed. The adjacent columna fornicis was also partly affected.

The other important nuclear groups of the hypothalamus were all well preserved. There was no involvement of the nucleus supra-opticus, the nucleus paraventricularis, the nucleus tuberis lateralis or the corpora mamillaria. All these cell groups were normal.

Myelin sheath stains revealed changes similar in all respects to those disclosed by the cell stains.

Case 2.—The greatest damage was found in the floor of the third ventricle, involving the substantia grisea and parts of the tuber cinereum just lateral to this area. The entire floor of the diencephalon was displaced upward by the pressure of the cyst from below, which produced a marked concavity in the floor. As in the preceding case, part of the floor of the third ventricle was torn away, leaving the third ventricle open to the spaces at the base of the brain. The entire substantia grisea was destroyed, very few cells remaining. There were hemorrhage, softening and perivascular infiltration in the floor of the third ventricle and in the tuber cinereum just adjacent to it. The perivascular cuffing was not primarily inflammatory but was probably secondary to the hemorrhage and softening. There was no meningitis. The floor of the tuber cinereum was partly destroyed, but this destruction extended only a short distance from the third ventricle and was very superficial, involving none of the hypothalamic nuclei. Sections stained by the Weigert method revealed demyelinization of the optic chiasm.

The nucleus paraventricularis, the nucleus supra-opticus, the nucleus tuberis lateralis and the tuberomamillaris and corpora mamillaria revealed no evidences of destruction.

COMMENT

In both cases reported death ensued, after an operation at the base of the brain, with a rapidily developing high degree of hyperthermia. The nature of the hyperthermia, with its steady upward trend, death within forty-eight hours and no appreciable drop, was characteristic of the temperature reaction following manipulation around the region of the pituitary gland in fatal cases.

The point of greatest interest from the standpoint of localization is the location of the pathologic changes in the region of the substantia grisea of the third ventricle, with destruction of the adjacent part of the tuber cinereum, and in case 1 of a small portion of the nucleus tuberomamillaris. All other hypothalamic nuclei escaped unharmed. The destroyed region in these cases corresponds closely with the area involved in the "subchronic" cats of Bazett, Alpers and Erb with loss of

temperature regulation. In these animals the infundibular nuclei of Winkler or the anterior hypothalamic nuclei of Rioch were found to be affected chiefly. While it is impossible to compare area for area the hypothalamic nuclei of the cat and of man because of definite structural differences in this region, it is possible nevertheless to indicate that the regions disturbed in the cases of hyperthermia reported here correspond closely with those found destroyed in cats without temperature control. In this sense, therefore, the findings are in good agreement, and the present cases indicate the great importance of the substantia grisea for the normal regulation of temperature.

The disturbing factor lies in the fact that in the case of the "subchronic" cats the temperature was always below normal, whereas in the cases reported here the temperature was decidedly above normal. The condition of the cats was characterized by evidences of severe impairment of the heat loss mechanism. This was not apparent in the cases reported here. It was not possible to determine the shivering response or the panting reaction in these patients. The clinical studies pointed rather away from the factor of heat loss. The problem becomes more complicated on consideration of other cases in which the lesions in this area have been carefully studied. Davison's[9] case of hypothermia was due to an angioma in the floor of the third ventricle which destroyed the tuber nuclei proper, parts of the supra-optic and paraventricular nuclei, the nucleus mamillo-infundibularis, the nucleus pallido-infundibularis and the substantia grisea centralis intercalatus and interfornicatus. While the destruction was much more extensive than in the cases reported here, it included the areas found to be destroyed in these cases. Foerster[10] observed hypothermia in two cases, one a case of tumor of the pituitary gland in which the patient had a rectal temperature of from 34 to 35 C. (93 to 95 F.) for weeks before death.

It seems clear, therefore, that in man, at any rate, lesions in the same region may produce either hypothermia or hyperthermia, and it also seems true that the area implicated in the production of hyperthermia in man is also involved in the loss of temperature regulation in cats. How may one explain the findings which seem to indicate that in the same area there may be predominantly evidence of heat production in one instance and of heat loss in another? Before attempting to answer this question it should be pointed out that both hypothermia and hyperthermia occur in cases of acutely developing lesions of the diencephalon, whether these lesions are due to tumor or to other causes. The production of hyperthermia may possibly be explained on the basis of

9. Davison, C., and Selby, N. E.: Hypothermia in Cases of Hypothalamic Lesions, Arch. Neurol. & Psychiat. **33**:570 (March) 1935.

10. Foerster, O.: Ueber Störung der Thermoregulation bei Erkrankungen des Gehirns und Rückenmarks, Jahrb. f. Psychiat. u. Neurol. **52**:1, 1935.

irritation. By this it is assumed that the areas responsible for the regulation of heat production were stimulated by virtue of irritant factors to an overproduction of heat, with probably a simultaneous impairment of heat loss mechanisms, though it is difficult to be absolutely certain of the latter.

There arises the further possibility that the same area, the substantia grisea of the third ventricle, is concerned with the power of temperature regulation and that this area, apparently of uniform histologic structure, contains centers for heat production and heat loss, either of which may, under conditions not entirely clear at the moment, be so damaged as to give rise under certain physiologic conditions to hypothermia and under others to hyperthermia. It is necessary to postulate, therefore, if this is true, that the same area may perform functions of a different nature under different conditions.

Or is it possible that in the region in question there is a small area which responds to cold, with sensory fibers from the cold receptors exaggerating their responses and those from the warm receptors inhibiting their responses? Injury of whatever sort might, then, by removing the "center" or the cold sensory tracts, produce hypothermia, whereas injury of the inhibitory warm fibers might permit the escape of heat and the production of hyperthermia. The latter response may be more readily produced in man, while the former seems to be more easily induced in cats.

There is still another possibility, suggested originally by Meyer,[11] that there are two separate centers, one for the production of heat, a so-called heat center, and another for the loss of heat, a so-called cold center. Meyer expressed the belief that regulation of temperature is due to the coordinate action of a sympathetic heat center and a parasympathetic cold center. He pointed out that sympathetic-stimulating drugs and toxins produce a rise in temperature, while parasympathetic toxins cause a decrease in temperature. The latter produce their effect through excitation of the cold center, a center which Meyer, incidentally, was unable to localize. Separate centers of this nature have been postulated more recently by Glaubach and Pick.[12] They found that animals in which the thalamus and collicular areas were removed had high fever after a preliminary fall of temperature, differing radically from hypothalamic animals, which react to their environmental temperatures. Glaubach and Pick expressed the belief that in diencephalic animals a temperature regulation center in the hypothalamic area is removed, and

11. Meyer, N. H.: Stand der Lehre vom Sympatheticus, Deutsche Ztschr. f. Nervenh. **45**:330, 1912.

12. Glaubach, S., and Pick, E. P.: Ueber zentrale Temperaturregulierung nach Ausschaltung des hypothalamischen Wärmzentrums, Arch. f. exper. Path. u. Pharmakol. **173**:571, 1933.

that when this occurs a cold center in the collicular area is inhibited and cannot act. This permits the thermogenetic center in the caudal parts of the brain to come into play. They believe apparently that there is a thermogenetic center in the hypothalamus and a cold center in the collicular area. While it is possible that separate centers exist, they still do not explain why such different responses may arise from lesions in the same area. The answer may possibly be found in the future disclosure that in man, at any rate, the mechanism controlling the loss of heat is more widely and differently located in the hypothalamus than that controlling the production of heat. Judging by the cases here recorded, the heat-producing area seems to be in the substantia grisea of the third ventricle.

SUMMARY

The cases of two patients who died with hyperthermia are reported.

Both revealed lesions in the substantia grisea of the third ventricle, corresponding to the areas involved in cats with loss of temperature regulation.

DISCUSSION

DR. STEPHEN WALTER RANSON, Chicago: The two cases described by Dr. Alpers emphasize well the importance of the hypothalamus for the regulation of heat. They are of particular interest to me because of some experiments which I have been doing with monkeys. It has been found that bilateral symmetrical lesions, destroying on both sides the posterior portion of the lateral part of the hypothalamus, that is, the region lateral to the mamillary bodies, cause in monkeys a profound loss in the capacity to maintain body temperature. The rectal temperature of these animals will drop as low as 94 F. if they are placed in a room with a temperature of from 70 to 75 F. The monkeys in my experiment were kept in a room with the temperature regulated at 86 F. There were nine of these animals and in all the lesions were located in the same situation. What is more pertinent to this particular discussion is that in seven monkeys in which the lesions were placed a little too far forward, the lesions being bilaterally symmetrical in the lateral part of the hypothalamus between the optic chiasm and the mamillary bodies, there occurred within a few hours after the operation a rather sharp rise in temperature, the temperature rising to 105.5, 105 and 106 F. and in one case to 106.5 F. These animals were kept at ordinary room temperature, and within from twenty-four to forty-eight hours their temperature dropped to normal and they were able to maintain it at normal under these conditions. It is useless to speculate at the moment on the interpretation of these experimental observations, except to say that they fall in line with Dr. Alpers' suggestion that postoperative hyperthermia may be due to an irritative lesion, that is, to irritation from a lesion which is near to but does not destroy the heat-regulating mechanism. Lesions lateral to the mamillary bodies cause loss of heat as a result of the destruction of this mechanism, while irritation by lesions a little farther forward appears to have been responsible for the postoperative hyperthermia in the animals.

DR. WILDER PENFIELD, Montreal: Can one draw an exact analogy between the hyperthermia observed clinically and that which one sees experimentally in animals? It has been my experience that animals really show poikilothermia. Dr. Erickson and Dr. Grant have each made a long-continued effort to reproduce human hyper-

thermia in animals, without success. The temperature will rise or fall, depending on the animal's environment. In man there is, as every neurosurgeon knows to his regret, a condition of true hyperthermia which, as Dr. Alpers has pointed out, is apt to develop after interference with the base of the brain. In such cases the hyperthermia is not the only important element. There is also hyperpnea and a very rapid pulse. The patient's temperature can be kept down artificially, and yet death may ensue with little control over the other phenomena.

Clinical hyperthermia, hyperpnea and tachycardia usually go together. But I have seen hyperpnea without hyperthermia. It has seemed to me from watching such patients die that for the most part the cause of death is true heart failure. The heart seems to be driven at such a terrific rate that in about thirty-six hours, as a rule, the patient dies from heart failure. For that reason, and considering the whole condition to be produced by a sort of malignant reflex, if one can use such a term (an irritation, as Dr. Alpers has called it), I have employed sedatives in small doses, using morphine, 1/32 grain (0.002 Gm.), or other sedatives, with considerable help. On the assumption that there is a reflex that one wants to inhibit, the sedatives are repeated frequently, with considerable benefit. Every effort must be made to cool the patient artificially as well.

Dr. Bernard J. Alpers, Philadelphia: With regard to Dr. Ranson's animals, recently Dr. Lewy and I made lesions with the Horsley-Clarke instrument mesially in the diencephalon in the hypothalamic region of animals and found that this area in general will produce a definite hypothermia. The lateral hypothalamic area does not seem to be of such great importance, although I think it is important to recognize that there is a quantitative difference in lesions in different portions of the anterior part of the hypothalamus. The more mesial lesions seem to produce a more marked effect and others a less marked effect.

OLIVOPONTOCEREBELLAR ATROPHY

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As has been emphasized elsewhere,[1] the classification of the cerebellar atrophies of Marie, Foix and Alajouanine [2] as congenital, familial and acquired is the most workable. Some forms of cerebellar atrophy, as for instance sclerotic, which is also known by other names,[1] possess distinct pathologic features, but the clinical picture may be so indefinite and obscure that they often remain clinically unrecognized. Conversely, other types, especially the hereditary and familial, generally known as heredocerebellar ataxia of Pierre Marie,[3] have a pronounced clinical but, as is generally assumed, an altogether indefinite pathologic picture. Thus, this exquisitely familial and hereditary morbid condition may occur as a combined degeneration of the cerebellum, pons and medullary olives, that is, as olivopontocerebellar atrophy which, according to Dejerine and André Thomas,[4] Loew [5] and others, is neither hereditary nor familial. However, a number of cases of olivopontocerebellar atrophy have been reported, usually under different names, in which both the familial and the hereditary characteristics were prominent. A most remarkable instance was reported by Keiller,[6] who followed up this form of cere-

From the Division of Neuropathology, University of Illinois College of Medicine.

Read at the Sixty-First Annual Meeting of the American Neurological Association, Montreal, Canada, June 4, 1935.

1. Hassin, G. B.: Sclerotic Atrophy of the Cerebellum, Arch. Neurol. & Psychiat. **31**:1205 (June) 1934; Crossed Atrophy of the Cerebellum, ibid. **33**:917 (May) 1935.

2. Marie, P.; Foix, C., and Alajouanine, T.: De l'atrophie cérébelleuse tardive à prédominance corticale (atrophie parenchymateuse primitive des lamelles du cervelet; atrophie paléocérébelleuse primitive), Rev. neurol. **38**:849 and 1082 (July) 1922.

3. Marie, Pierre: Sur l'hérédo-ataxie cérébelleuse, Semaine méd. **13**:444, 1893.

4. Dejerine, L., and Thomas, André: L'atrophie olivo-ponto-cérébelleuse, Nouv. iconog. de la Salpêtrière **13**:330, 1900.

5. Loew, P.: L'atrophie olivo-ponto-cérébelleuse (type Dejerine-Thomas), Paris, G. Steinheil, 1903.

6. Keiller, W.: Four Cases of Olivo-Ponto-Cerebellar Atrophy Giving a History of Heredity with Three Autopsies, South. M. J. **19**:518 (July) 1926.

bellar atrophy in ten members of four generations of a Southern Negro family. The central nervous system of two patients and the spinal cord of a third have also been studied by Keiller pathologically. The results of examination of the brain of the third patient, which had been preserved as a museum specimen for ten years, and of a restudy of Dr. Keiller's stained and mounted sections are the subject of the present contribution. In all three cases the changes in the central nervous system were alike and typical of olivopontocerebellar atrophy. Clinically, the conditions presented were also alike and typical of what Pierre Marie described as heredocerebellar ataxia. Studies of the three cases and of the literature permit a conclusion that heredocerebellar ataxia and olivopontocerebellar atrophy are one disease process.

REPORT OF CASES

We are able to give short histories of the cases of only five of the ten members of the family, compiled from Dr. Keiller's paper.

CASE 1.—John A., who died at the age of 35, showed the first symptoms at the age of 14. The disease thus lasted for twenty-one years and was especially severe during the last nine years. The early symptoms were: lack of coordination, staggering gait and choreiform movements in the "legs, arms, head and body."

Examination by the family physician (Dr. Jones) revealed marked bilateral intention tremor and general shaking of the body, which persisted in sleep. The head exhibited continuous "nodding and rotary movements," and speech was markedly dysarthric. There was difficulty in forming words, especially "linguals, labials and dentals." Chewing and swallowing were not affected, nor were the mental condition and the visceral organs disturbed. Toward the end of the disease the patient suffered from urinary incontinence, cardiac decompensation and bed sores.

CASE 2.—William A., brother of John A., died at the age of 32. He suffered much in the same way as did John, so that the same history can be applied to both. Toward the end of life a bronchial condition developed which "may have hastened his death." In disposition the patient was amiable, in contrast with his brother John, who was rather irritable. As to the condition of the reflexes, there is a brief note that "Babinski and other reflex tests could not be made." The duration of the advanced symptoms was, as in the previous case, about nine years.

CASE 3.—Joe E., a nephew of John and William by a sister, died at the age of 37; like his uncles he suffered markedly for about nine years from "identical" symptoms.

CASE 4.—Henrietta M., a sister of Joe E., aged 33, was married at 20 and had a son, aged 16, who was said "to be in good health" (this could not be verified as the boy lived in another state). At the age of 15 the patient had undergone hysterosalpingo-oophorotomy and appendectomy. At the age of 31 she began to suffer from weakness in the knees, a tendency to wobble in walking and a general shaking of the whole body, especially the arms. Examination (by Dr. Keiller, on Dec. 2, 1924) showed: "The patient was fat, good natured, responsive and able to do a good deal of housework. Her whole body showed

trembling movements, rather a coarse general tremor than choreiform movements. She got about the house fairly well by holding on to many available supports. There was no asthenia, hypotonia, incoordination or adiadokokinesis. There was some dysmetria—a slight 'overmeasuring in touching the physician's finger.' The patient could not bend backward without losing her balance; she could not stand on one foot, and there was some unsteadiness when she got up from a seat."

The cranial nerves were normal; nystagmus was not present.

The plantar reflex was very poor and seemed slightly extensor; there was no Gordon or Oppenheim reflex. In speaking, consonants were not articulated. There were no other apparent defects of speech.

In November 1925, "approximately one year after the last examination," the patient "was fat and looked well." Her muscles were firm. All symptoms had decidedly progressed. The tremors were more marked. She had considerable difficulty in arising from a seat; she "walked with many tremors; showed considerable dysmetria and tremor in drinking a glass of water and touched the physician's finger very awkwardly with the palm of her hand. Her speech was markedly slurring."

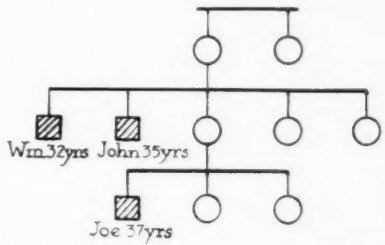

Fig. 1.—The shaded circles indicate the cases studied pathologically; the rest, the cases that presented a clinical picture of heredocerebellar ataxia.

CASE 5.—Mary, a younger sister of Henrietta (case 4), aged 28, undoubtedly showed early symptoms—"a suspected tremor;" one year later there was a "decided intention tremor and cerebellar gait."

Comment.—No detailed information could be obtained relative to the other members of the family, some of whom suffered from a similar malady. It was asserted by the patients that the mother of William and John, their maternal aunt, and three sisters and three children of one of the latter all exhibited an identical clinical picture, which set in comparatively late in life. The affliction was thus decidedly hereditary and familial (fig. 1).

Fragmentary as the histories are, they mention the signs and symptoms that commonly occur in Marie's heredocerebellar ataxia. They were: cerebellar gait, disturbances of equilibrium, incertitude of movements (incoordination), disturbances of speech, tremor of the head and lively reflexes. No visual disturbances were recorded but, according to Londe,[7] these need not occur in this type of cerebellar ataxia.

Macroscopic and Microscopic Examinations.—The gross appearance of the brain, cerebellum, pons and medulla are shown in figure 2. The cerebellum, pons and medulla were reduced in size; the occipital lobes protruded over the cerebellum, the lamina of which appeared greatly shrunken. The picture also shows loose cerebellar laminae. The frontal lobe was atrophied, and the meninges were

7. Londe, P.: L'hérédo-ataxie cérébelleuse, Presse méd. **3**:385, 1895.

opaque, especially over the temporal lobe. Keiller also emphasized the presence in the brains he studied of some atrophy of the cerebral convolutions, especially of the frontal and superior temporal lobes. Though, as said, the brain had been kept for ten years as a museum specimen, some staining methods (for the myelin fibers, axons and neuroglia) gave fairly good results.

Some leaflets of the cerebellum were normal; others exhibited marked degeneration of the white substance (fig. 3). A few nerve fibers were preserved and separated from one another by bands of glial tissue (fig. 4). The latter consisted of fibrillary astrocytes and glia fibers, which followed the course of the extinct nerve fibers, giving a picture of isomorphous gliosis. The degenerated areas, transformed into a glial tissue scar, were immensely rich in blood vessels, some of which were newly formed and possessed thickened hyperplastic walls.

Fig. 2.—A photograph of the brain, cerebellum, pons and medulla. The atrophied cerebellum is overlapped by the occipital lobes.

Though the white substance of the leaflets was much degenerated, there were always present healthy myelin fibers, often as naked axons (fig. 4). Other white fibers, such as the U-shaped fibers connecting two neighboring lamellae (arcuate, associate fibers), were not affected. It must therefore be assumed that the degeneration involved mainly centripetal (cerebellopetal) or afferent fibers that reached the cerebellum through the middle cerebellar peduncles. Probably some of the degenerated fibers were also efferent, centrifugal or projection fibers which originated in the cerebellar cortex.

The degeneration of the cerebellar white substance was the most outstanding change noted. It was in the nature of terminal nerve degeneration, the completely degenerated nerve parenchyma being replaced by a glial tissue scar, which is well shown in figure 4 among the retained nerve fibers.

Much milder but less constant were the changes in the cortical layers of the cerebellum—the granular, that of the Purkinje cells and the molecular. The

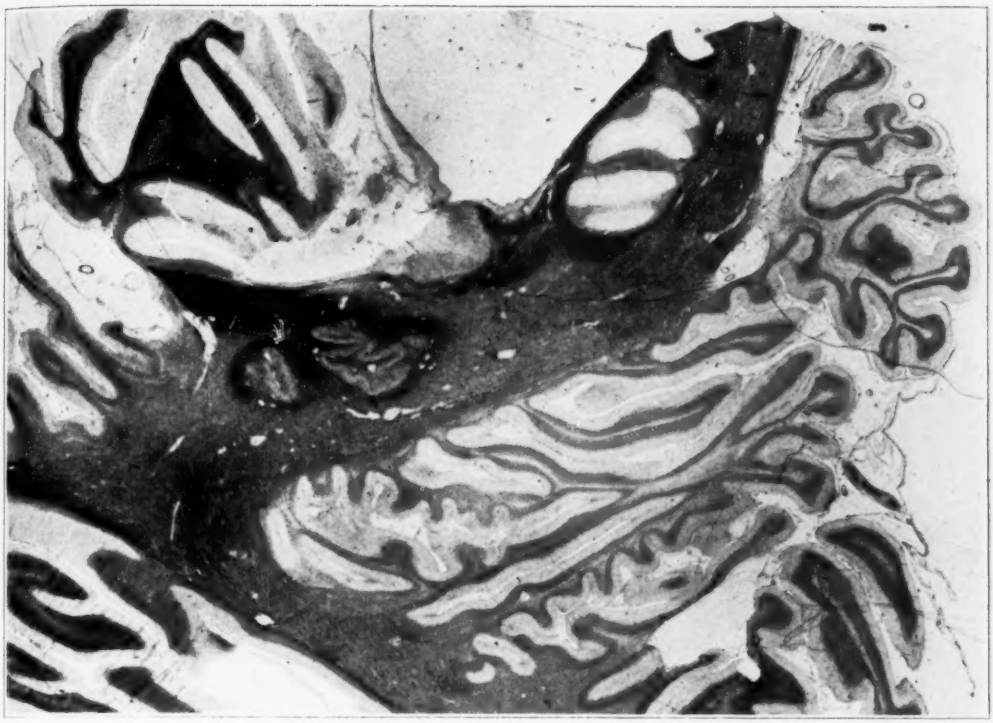

Fig. 3.—This section shows the atrophied lamellae of the cerebellum. The unstained cores of the lamellae of the white substance are shown under higher magnification in figure 4. Pal-Kultschitzky stain.

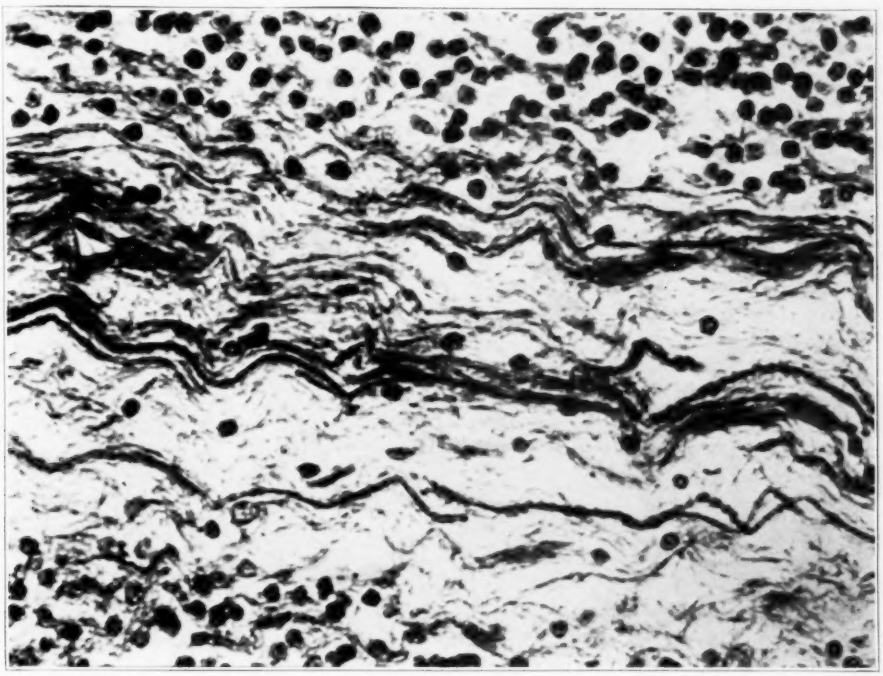

Fig. 4.—In this section the white substance, between the granular layers, is represented by a few axons crossing a broad band of a glial tissue scar. Bielschowsky stain.

granular layer, which borders on the white substance, the "core" of the laminae, was well preserved. Only occasionally did it appear slightly rarefied. It appeared as a dense band and was always well stained (fig. 4), in marked contrast with what is seen in the sclerotic and crossed atrophies of the cerebellum, in which this ganglion cell layer is completely degenerated and devoid of constituent cells (granular, Golgi [type II] cells) and of the climbing and intragranular or mossy fibers. In the present cases the latter were only partly degenerated.

The layer of Purkinje cells was variably affected. In some leaflets the Purkinje cells were reduced in number; in others they were preserved, and in some they were lacking entirely (fig. 5 *B*). They usually exhibited climbing and basket fibers, but occasionally the baskets were devoid of contents, and the Purkinje cells appeared as a row of empty baskets (fig. 6 *B*). The layer of Bergmann's glia cells, in which the Purkinje cells are embedded, was always well developed.

The molecular layer was appreciably reduced in width; it contained few stellate cells and nerve fibers, while glial tissue and blood vessels were abundant.

The pia over the molecular layer was moderately hyperplastic. Over the cerebrum the subarachnoid space was distended, and its meshes were filled with lymphocytes, fibroblasts and mesothelial cells.

The changes outlined were not found in the flocculus or amygdalae, and only to some extent were they present in the vermis. Contrasting the photomicrographs in figure 5, one can see in *A* (flocculus) well developed nerve fibers (*W. S.*) streaming from the brachium pontis to the cerebellum; in *B* (the semilunar lobe) such fibers are not seen. They were destroyed and replaced by a glial tissue scar (*Scl.*). The granular layer in the flocculus (*A*) was rich in ganglion cells and mossy fibers, which were very scarce in the semilunar lobe (*B*), causing its rarefaction. The molecular layer in the flocculus was rich in arborizations of the Purkinje and other ganglion cells, whereas in the semilunar lobe they were scarce. Neuroglial tissue often appeared as a broad band in the semilunar lobe, but in comparison was scarce in the flocculus. The changes in the amygdalae were like those in the flocculus; in the quadrilateral lobe they resembled those of the semilunar lobe. The lower vermis was only slightly affected.

Pons: As noted, the pons appeared atrophied, even macroscopically. Its transverse fibers (upper, middle and lower), including those of the brachium pontis (middle cerebellar peduncles), were discolored in specimens stained with the method of Pal and Kultschitzky (fig. 7). Even in such specimens, however, it was possible to discern under higher magnification a number of myelinated fibers that were well stained. However, such fibers never appeared as bright and as large as the normal longitudinal pyramidal fibers (fig. 7). They resembled also the perfectly normal structures of the tegmentum of the pons—the fillets, the brachium conjunctivae, the posterior longitudinal bundle, the central tectal pathways and the roots of the fifth nerve (fig. 7).

Microscopically, the demyelinated areas of the base of the pons occasionally exhibited naked axons—nerve fibers deprived of their myelin sheaths. Some nerve fibers still retained their myelin, but the majority were replaced by cytoplasmic and fibrillary glia and lacunae which contained collapsed blood vessels. Ganglion cells, normally so numerous in the pontile meshes formed by transverse and longitudinal nerve fibers, were exceedingly scarce, and only occasionally was a stray ganglion cell encountered, which was shrunken and sclerosed. The rest of the ganglion cells were replaced by glial tissue, blood vessels and lacunae. On the whole, the microscopic changes of the pons were analogous to those of the sclerosed parts of the cerebellum already described.

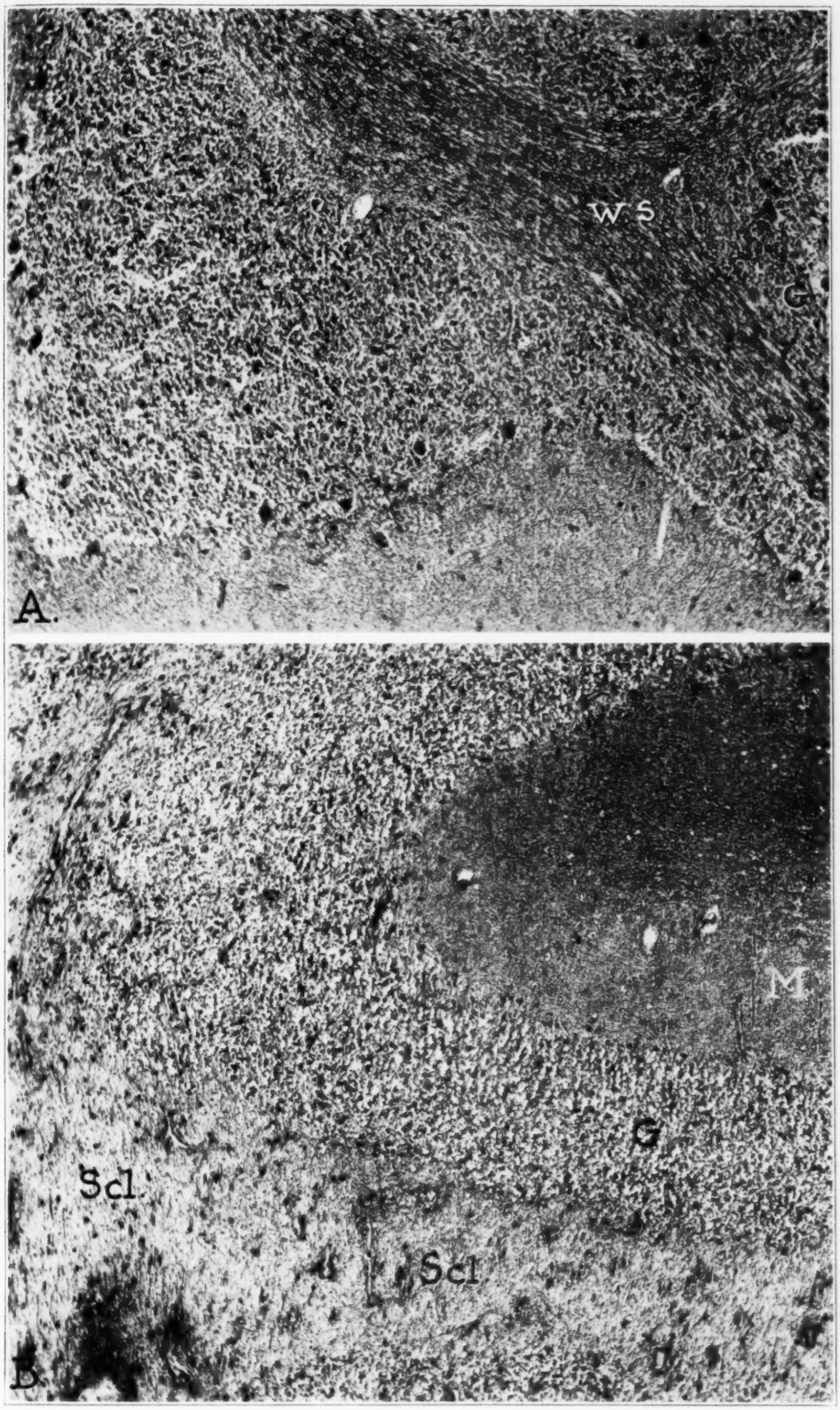

Fig. 5.—In *A*, a photomicrograph of the flocculus, the tree layers and the core show no changes, nor is the molecular layer particularly changed. *W.S.* indicates the white substance; *G*, the granular layer. In *B*, a photomicrograph of the semilunar lobe, Purkinje cells, so well shown in *A*, are absent; the white substance is replaced by a glial scar (*Scl.*). *M* indicates the molecular layer; *G*, the granular layer, rarefied in the left half of the picture, and *Scl.* an area of sclerosis.

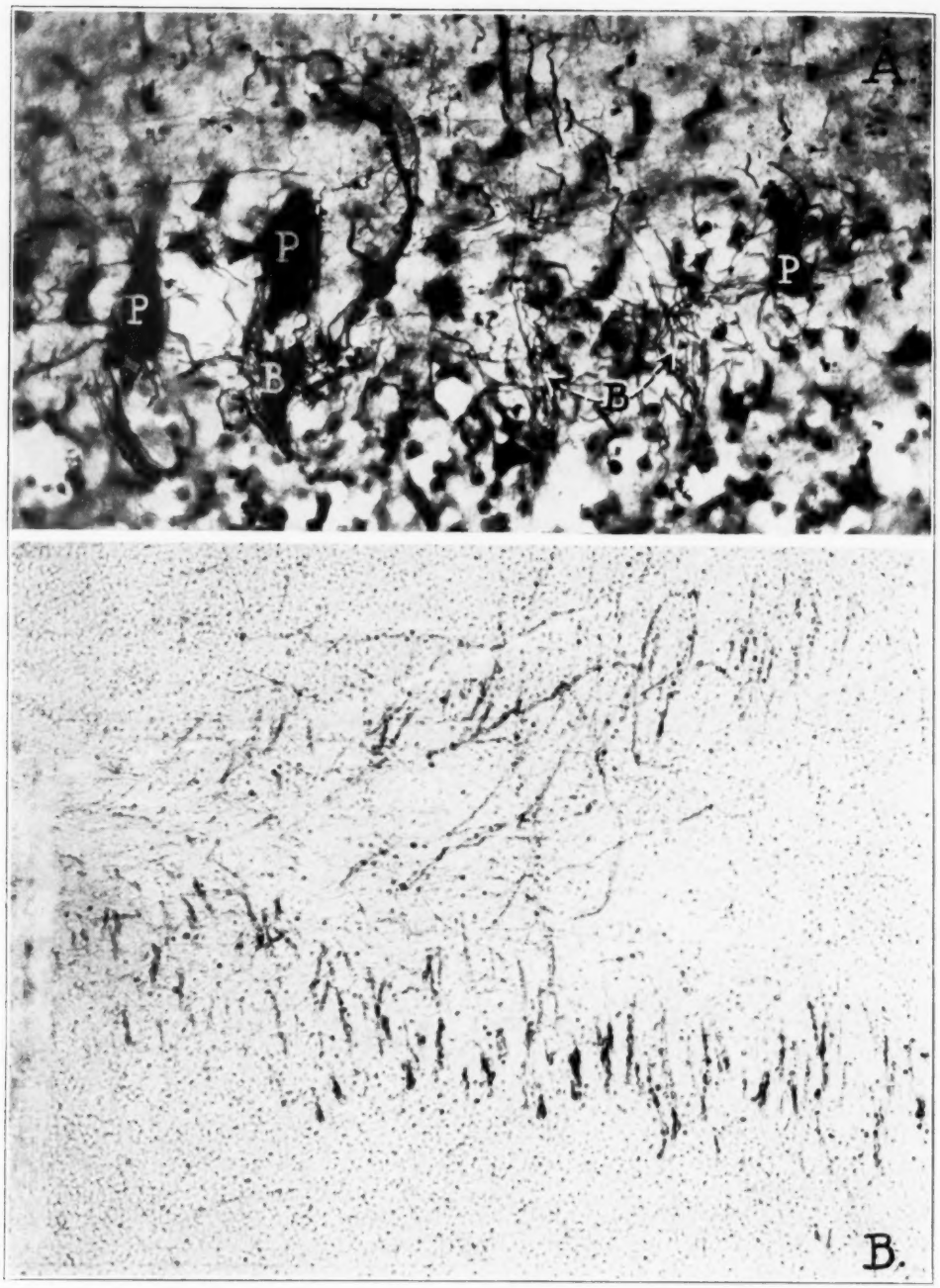

Fig. 6.—In section *A* the baskets (*B*), one at the base of the Purkinje cells (*P*) and two indicated by arrows, are empty; an apical dendron to the right of the middle *P* is accompanied by a climbing fiber. Section *B* shows numerous empty baskets in rows (under low power). Bielschowsky stain.

Medulla Oblongata: Like the cerebellum and pons, the medulla was reduced in size and exhibited macroscopic and microscopic changes. These were especially evident in the olivary bodies (including the accessory olives), the olivocerebellar fibers, the fibers of the hili of the main olives, the ventral arcuate and periolivary nerve fibers and those of the central part of the restiform bodies and the acoustic or medullary striae (fig. 8). The degeneration of the foregoing nerve fibers was, of course, secondary to that of the ganglion cells of the olivary bodies and the arcuate nuclei. Few ganglion cells were present in the olives or arcuate nuclei. Those that were preserved were greatly reduced in size; they were shrunken, sclerosed and devoid of processes. Like the pons, the larger portion of the olives was transformed into a glial tissue scar and exhibited numerous lacunae enclosing shrunken, collapsed blood vessels.

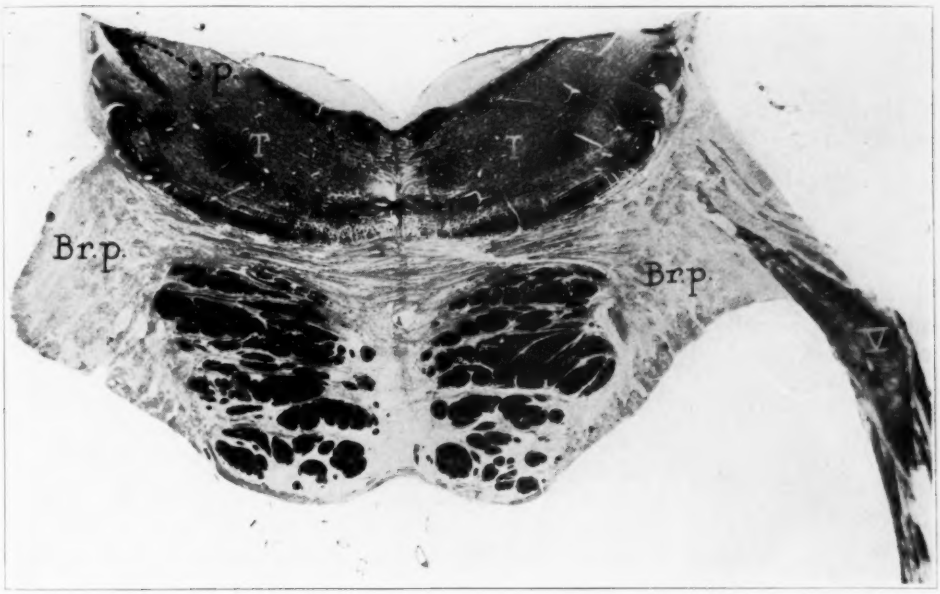

Fig. 7.—In this section of the pons *Br. p.*, the brachium pontis (middle cerebellar peduncles), and the transverse fibers are degenerated; the dark masses are normal pyramidal fibers. The tegmentum of the pons (*T*) is normal, including the superior cerebellar peduncle (*s.p.*); *V*, the fifth cranial nerve (normal). Pal-Kultschitzky stain.

Structures in the pons and medulla which had no anatomic connection with the ganglion cells of the pons, arcuate nucleus and olivary bodies (the lemnisci, descending root of the fifth nerve, bulbar nerves, etc.) were not affected.

Spinal Cord: The spinal cord could be studied only in the case of Joe, in specimens prepared by Dr. Keiller. There was mild rarefaction in the posterior and marked rarefaction in the lateral column of one side. In the former, the middle root zone of Flechsig and the entrance root zone exhibited slight degeneration of nerve fibers, while in the lateral column the pyramidal fibers and the dorsal spinocerebellar tract were asymmetrically involved. In both columns the distribution of degenerated areas resembled that in Friedreich's ataxia, but it

was less intensive and extensive. No noteworthy changes were present in Gowers' tract. In some areas the degeneration was limited to small bands of fibers. In specimens stained with hematoxylin and eosin or by the silver method of Bielschowsky, the affected areas showed fibrillary and cytoplasmic astrocytes and also lacunae harboring collapsed, hyperplastic blood vessels, the walls of which were often infiltrated with gitter cells and lymphocytes (fig. 9). No gitter cells or inflammatory phenomena were found elsewhere in the affected areas, which all exhibited extreme degeneration. The lacunae were present in both the gray and the white substance as large cavities and were especially numerous in the posterior columns, where blood vessels were very abundant.

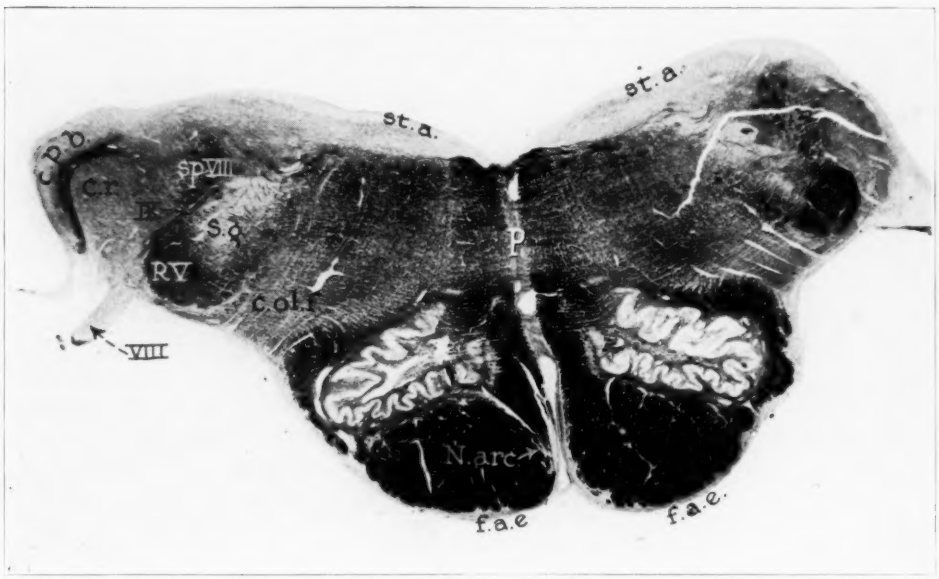

Fig. 8.—In this section of the medulla the nucleus arcuatus (*N.arc.*) and the external arcuate fibers (*f. a. e.*) are degenerated. The olivary bodies exhibit hardly any myelin fibers between the convolutions. The periolivary fibers are greatly diminished, and the olivocerebellar fibers (*c. ol. f.*) are degenerated. *VIII* indicates the eighth nerve; *c.p.b.*, the corpus pontobulbare of Essick; *c.r.*, the corpus restiforme, which is degenerated excepting the dark crescent which is the only normal remnant of the corpus restiforme; *IX*, the ninth nerve, which is not crossed by the cerebello-olivary fibers; *R.V.*, the descending root of the fifth nerve, which is not crossed by the cerebello-olivary fibers (these are degenerated); *S.g.*, the substantia gelatinosa Rolandi; *st.a.*, the stria-acusticae, which are degenerated, and *P*, the fibers of Piccolomini, which are degenerated. Pal-Kultschitzky stain.

Definite changes were present in the posterior roots, in which some nerve fibers were degenerated. The pia mater was hyperplastic and thickened but not infiltrated.

Cerebrum: The ganglion cells of the cortical layers of the cerebrum were somewhat swollen, without phenomena of neuronophagia or satellitosis. In general, the cerebral cortex, as well as the mesencephalon and diencephalon, exhibited

no significant changes. Only in the cerebral peduncles were lacunae in evidence; these were not so numerous as in the pons, medulla and cerebellum.

Summary of Gross and Microscopic Changes.—There were: diminished size of the cerebellum, pons and olives; advanced degeneration of the ganglion cells of the olives, arcuate nuclei, basal portion of the pons and, to a much lesser extent, of the stellate and Purkinje cells of some leaflets of the cerebellum, with occasional formation of empty baskets; degeneration of olivocerebellar fibers, inner portion of the restiform bodies, external arcuate fibers, middle cerebellar peduncles

Fig. 9.—In this section of the spinal cord the lacunae contain many collapsed and hyperplastic blood vessels.

(brachium pontis), white substance of some cerebellar folia; occasional degeneration of climbing and mossy fibers, and mild degeneration of the posterolateral columns and posterior roots of the spinal cord.

COMMENT

Of the changes described, the outstanding were: atrophy of the olives, the pons and the white substance of some cerebellar lamellae—a combined atrophy generally known as the olivopontocerebellar type. The significance of the microscopic changes outlined can better be understood when they are contrasted with a degenerative condition in which only

the cortex of the cerebellum is involved, known as lamellar, sclerotic [1] or late cortical cerebellar atrophy. Here there is an extensive and intensive primary destruction of some or all the ganglion cells of the various cerebellar layers (Purkinje, granular, stellate, basket and Golgi [type II] cells) and of the nerve fibers ensuing from these cell groups. It is a vast efferent, cerebellofugal atrophy. In olivopontocerebellar atrophy there is also a vast destruction of ganglion cells, but of those of the medullary olives, arcuate nuclei and pons. The degeneration of the nerve fibers ensuing from these cells is toward the cerebellum; it is afferent or centripetal. The atrophied nerve fibers extending to the cerebellum appear there as a sclerosed white substance (*Scl.*) and are therefore the principal if not the only cause of the reduced size of the cerebellum. The Purkinje and other ganglion cells of the cerebellar cortex may also become affected, but not to the extent seen in primary cerebellar atrophy (sclerotic or lamellar, etc.). Thus, the majority of leaflets exhibited an entirely normal cortex (fig. 5*A*), and if some Purkinje cells were missing it was not possible to demonstrate manifest reactive glial phenomena. In some cases (Schweiger,[8] van Bogaert and Bertrand [9] and others) atrophy of the cortical cells of the cerebellum was absent. The inconstant occurrence of atrophy of the cerebellar ganglion cells in olivopontocerebellar atrophy, the disproportion between the meager number of such degenerated cells and the vast destruction of the pons and medulla can be understood only on the assumption that the atrophy of the cerebellum in this morbid condition is not primary, as was considered by von Stauffenberg [10] and Kufs [11] and partly by Dejerine and Thomas [4] and others. Neither is it an inflammation or a vascular disease process, as was thought by Arndt,[12] but it is secondary to a primary degeneration of the pons and olivary bodies. Such an extensive atrophy as is presented in figures 7 and 8 certainly could not be caused by destruction of a few Purkinje cells. On the contrary, the Purkinje cells themselves evidently became affected as the result of retrograde or transsynaptic (van Bogaert and Bertrand [9]) degeneration brought on by massive destruction of the afferent pontile and olivocerebellar nerve fibers.

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8. Schweiger, L.: Zur Kenntnis der Kleinhirnsklerose, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **13**:260, 1906.

9. van Bogaert, L., and Bertrand, I.: Une variété d'atrophie olivo-pontine à évolution subaiguë avec troubles démentiels, Rev. neurol. **1**:165, 1929.

10. von Stauffenberg: Zur Kenntnis des extrapyramidalen motorischen Systems, und Mitteilung eines Falles von sogenannter "Atrophie olivo-ponto-cérébelleuse," Ztschr. f. d. ges. Neurol. u. Psychiat. **39**:1, 1918.

11. Kufs, H.: Ueber einen Fall von Atrophia olivo-cerebellaris auf der Basis einer luetischen Frühmeningitis mit nach 8-½ Jahren nachfolgender progressiver Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **96**:275, 1925.

12. Arndt, Max: Zur Pathologie des Kleinhirns, Arch. f. Psychiat. **26**:404, 1894.

While it is conceded that olivopontocerebellar atrophy is a well defined pathologic entity, it is generally thought to be devoid of typical clinical features, for clinically it hardly differs from heredocerebellar ataxia of Marie. Absence of hereditary and familial traits was emphasized by Dejerine and Thomas,[4] Loew,[5] Neff [13] and others as the cardinal feature of olivopontocerebellar atrophy, a feature in which it is supposed to differ from the type of Marie. Our cases and similar ones in the literature (Winkler,[14] for instance) prove that such a clinical difference between the "two types" does not exist, that the olivopontocerebellar type described by Dejerine and Thomas is often both hereditary and familial. Neither do the two types differ pathologically. Switalski,[15] Thomas and Roux [15a] and Rydel,[15b] for instance, described the changes in three cases of Klippel and Durante,[16] which were some of the cases on which Pierre Marie based the formulation of his new morbid entity, as follows: definite smallness of the cerebellum, pons and medulla; degeneration of the superficial and middle pontile fibers, of the spinocerebellar tracts and of Clarke's column and the posterior columns; badly stained, but not degenerated, restiform and olivary bodies, and well preserved ganglion cells of the pons. The majority of the enumerated changes emphasized by Switalski are certainly typical of olivopontocerebral atrophy. Even more definite is the latest description by Mathieu and Bertrand.[17] These authors mentioned atrophy of the cerebellum, especially of its upper surface; sclerosis of both bulbar olives; atrophy of the nuclei of the pons, with mild degeneration of its transverse fibers; degeneration of the spinocerebellar tracts and ventrolateral columns, and intactness of the posterior columns. Mathieu and Bertrand stated definitely that "at certain segments a veritable aspect of olivopontocerebellar atrophy obtains." A somewhat similar view was expressed by Hänel and Bielschowsky,[18] who included

13. Neff, I. H.: A Report of Thirteen Cases of Ataxia in Adults with Hereditary History, Am. J. Insanity **51**:365, 1894-1895.

14. Winkler, C.: A Case of Olivo-Pontine-Cerebellar Atrophy and Our Conceptions of Neo- and Palaio-Cerebellum, Schweiz. Arch. f. Neurol. u. Psychiat. **13**:684, 1923.

15. Switalski: Sur l'anatomie pathologique de l'hérédo-ataxie cérébelleuse, Nouv. iconog. de la Salpêtrière **14**:373, 1901.

15a. Thomas, A., and Roux, J.: Sur une forme d'hérédo-ataxie cérébelleuse, à propos d'une observation suivie d'autopsie, Rev. de méd., Paris **21**:762, 1901.

15b. Rydel, A.: Sur l'anatomie pathologique d'une forme d'hérédo-ataxie cérébelleuse, Nouv. iconog. de la Salpêtrière **17**:289, 1904.

16. Klippel and Durante, G.: Contribution à l'étude des affections nerveuses familiales héréditaires, Rev. de méd., Paris **12**:745, 1892.

17. Mathieu, P., and Bertrand, I.: Études anatomocliniques sur les atrophies cérébelleuses, Rev. neurol. **1**:721, 1929.

18. Hänel, H., and Bielschowsky, M.: Olivocerebellare Atrophie unter dem Bilde des familiären Paramyoclonus, J. f. Psychol. u. Neurol. **21**:385, 1915.

their case as one of olivocerebellar form, while Holmes [19] asserted that in the majority of cases progressive cerebellar disease belongs to the class of olivopontocerebellar atrophy, adding that no form of disease exists to which the term "heredocerebellar ataxia" can be aptly applied. Finally, Marie, Foix and Alajouanine themselves,[2] in discussing the differential diagnosis between late cerebellar cortical and olivopontocerebellar atrophies, stated that though there are gross differences there is probably also some relationship (*des parentés*) present between the two morbid conditions. Pathologically, it is evidenced by the presence of a partial degeneration of the olives, the importance of which changes, they believed, should not be exaggerated but also not ignored.

Careful analysis of the cases recorded as instances of heredocerebellar ataxia of Marie forces one to the conclusion that practically all such cases may be considered cases of olivopontocerebellar atrophy. Guillain, Mathieu and Bertrand [20] frankly stated (page 449 of their article) that there is no fundamental clinical difference between the foregoing morbid entities. The old cases of Fraser,[21] Schultze,[22] Menzel,[23] Nonne,[24] Sanger Brown,[25] Arndt, Miura,[26] Schuster [27] and others also were instances, in our opinion, of olivopontocerebellar atrophy. In some of them there were observed also changes in the superior cerebellar and the dentate nucleus and in the nuclei of some bulbar nerves, but such additional changes were not manifested clinically. In general, the records of such cases were incomplete and unsatisfactory. For instance, Nonne [24] admitted that in his case only two small pieces (*Stückchen*) were studied,

19. Holmes, Gordon: A Form of Familial Degeneration of the Cerebellum, Brain **30**:466, 1907.

20. Guillain, G.; Mathieu, P., and Bertrand, I.: Étude anatomo-clinique sur deux cas d'atrophie olivo-ponto-cérébelleuse avec rigidité, Ann. de méd. **20**:417, 1926.

21. Fraser, D.: Defect of the Cerebellum Occurring in a Brother and Sister, Glasgow M. J. **13**:199, 1880.

22. Schultze: Ueber einen Fall von Kleinhirnschwund mit Degenerationen im verlängerten Marke und Rückenmarke (wahrscheinlich im Folge von Alkoholismus), Virchows Arch. f. path. Anat. **108**:331, 1887.

23. Menzel, P.: Beitrag zur Kenntnis der hereditärer Ataxie und Kleinhirnatrophie, Arch. f. Psychiat. **32**:160, 1891.

24. Nonne, M.: Ueber eine eigentümliche familiäre Erkrankungsform des Centralnervensystems, Arch. f. Psychiat. **22**:283, 1891; **39**:1225, 1905.

25. Brown, Sanger: On Hereditary Ataxia with a Series of Twenty-One Cases, Brain **15**:250, 1892.

26. Miura, K.: Ueber l'hérédo-ataxie cérébelleuse Marie's, Mitt. a. d. med. Fac. d. k.—jap. Univ. z. Tokio **4**:19, 1898.

27. Schuster, P.: Die im höheren Lebensalter vorkommenden Kleinhirnerkrankungen nebst Bemerkungen über den cerebellaren Wackeltremor, Ztschr. f. d. ges. Neurol. u. Psychiat. **91**:531, 1924.

one from the right cerebellar hemisphere and the other from the superior vermis. Both were normal. Probably *Stückchen* from other parts of the cerebellum would have shown changes either in some cortical layers or in the white substance of some of its lamellae. Though Nonne found the structure of the cerebellum, pons and medulla entirely "normal," he did not attempt to explain the cause of their smallness. It certainly was not due to the many fine "fibers" he found in the anterior spinal roots, nor could these fine fibers account for the clinical picture in his case. In the few cases that were better studied there were changes which were similar to those described in this paper. For instance, close analysis of the famous cases of Menzel [23] and Sanger Brown [25] discloses clinical and pathologic features of olivopontocerebellar atrophy. Menzel's patient and the patient's brother and sister suffered from tremors, incoordination, speech difficulties, ataxia and other symptoms of cerebellar involvement. The brain and spinal cord of one patient were studied pathologically and revealed degeneration of the posterior columns and Flechsig's tract, atrophy of the medulla, olives, restiform bodies, pons (its ventral portion) and cerebellum, and preservation of the amygdalae, vermis and flocculus. On the whole, the microscopic changes were identical with those recorded in our cases. Sanger Brown's cases were observed in four generations of a white family, twenty-four members of which exhibited signs of cerebellar involvement—ataxia, staggering gait, disturbances of speech and vision and exaggerated knee jerks. The central nervous system of three members was studied pathologically; one by Adolf Meyer (1897) [28] and two by Lewellys Barker (1903).[29] Adolf Meyer found in the cerebellum a slight reduction of Purkinje cells, hardly any atrophy of the cerebellar folia and a normal number of ganglion cells in the olivary bodies, but an increase in the neuroglia tissue, with numerous amyloid bodies. In addition, there was degeneration of the posterior columns and the direct spinocerebellar tract. Though the tissues were poorly preserved and were evidently difficult to study, it was possible to bring out some changes in the Purkinje cells and olivary bodies (increase in glia and amyloid bodies), that is, manifestations of olivocerebellar atrophy, aside from changes in the spinal cord. In Barker's case (the eighteenth member of the family) the medulla and pons were reduced in size; the stratum interolivare leminisci contained thinned nerve fibers; the arcuate nuclei were small; the gray

28. Meyer, Adolf: The Morbid Anatomy of a Case of Hereditary Ataxia, Brain **20**:276, 1897.

29. Barker, L.: A Description of the Brains and Spinal Cords of Two Brothers Dead of Hereditary Ataxia: Cases XVIII and XX of the Series of the Family Described by Sanger Brown, with a Clinical Introduction by Sanger Brown, Decennial Publications of the University of Chicago, Chicago, University of Chicago Press, 1903, vol. 10, p. 349.

matter of the inferior olives and their ganglion cells were also somewhat diminished in number. The olivocerebellar fibers and the external arcuate fibers, corpus restiforme and pons were reduced in number and size, but the nuclei and the transverse and longitudinal fibers of the pons were normal. In the nucleus dentatus the ganglion cells were reduced at some levels to almost one-quarter the normal number. The cortical layers of the cerebellum were normal; the white substance was thinned. The flocculus was normal. In the spinal cord there was symmetrical degeneration of the midroot zone of Flechsig with a mild disease of the ventral root zone and almost complete degeneration of Flechsig's tract. In another member of the same family Barker found degeneration of the midroot zone of Flechsig in the posterior columns, complete degeneration of the direct spinocerebellar tract, probable degeneration of cells in the olives, a normal pons and a rather indefinite appearance of Purkinje cells. Barker emphasized that in both cases the degeneration involved chiefly the ganglion cells and nerve fibers of centripetal paths.

Among the interesting features of the condition in Barker's case are changes in the spinal cord, similar to those present in our cases, and absence of changes in the pons in his second case. Because of many other features already referred to, Barker's two cases may be included with those of olivopontocerebellar atrophy. They also show that aside from the typical cases of Dejerine and Thomas and Winkler and those recorded in this paper, there are some cases in which the lesions are incomplete or only partial. For instance, the pons and cerebellar cortex may appear entirely normal, or the pathologic picture may become complicated with other morbid conditions—multiple sclerosis (André Thomas [30]), encephalitis (Hammarberg [31]), paralysis agitans (Messing [32]), syphilitic meningo-encephalitis (Kufs [11] and Bielschowsky and Hirschfeld [33]) or extrapyramidal lesions (Mingazzini and Giannuli,[34] and Ley [35]). Mathieu and Bertrand [17] devoted a special study to combinations of olivopontocerebellar atrophy with other pathologic conditions, in which, the different lesions becoming superimposed on one

30. Thomas, André: Atrophie du cervelet et sclérose en placques, Rev. neurol. **11**:121, 1903.

31. Hammarberg, C.: Atrophie und Sklerose des Kleinhirns, Nord. med. ark **22**:31, 1890; abstr., Neurol. Centralbl. **11**:142, 1892.

32. Messing, Z.: Atrophie olivo-ponto-cérébelleuse dans un cas de maladie de Parkinson, Rev. neurol. **1**:498, 1930.

33. Bielschowsky, M., and Hirschfeld, R.: Zerebellare progressive Paralyse, J. f. Psychol. u. Neurol. **45**:185, 1933.

34. Mingazzini, G., and Giannuli, A.: Klinischer und pathologisch-anatomischer Beitrag zum Studium der Aplasia cerebro-cerebellospinalis, Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:521, 1924.

35. Ley, R.: Form atypique d'atrophie cérébelleuse ayant évolué en syndrome rigide, Arch. internat. de méd. expér. **1**:277, 1924-1925.

another, both pathologic and clinical features are obscured, rendering a proper interpretation of such cases difficult. In their case, for instance, olivopontocerebellar atrophy was combined with changes in the prefrontal and temporal lobes and degeneration of the tangential fibers, but the cerebellar cortex was intact.

Whether pure or complicated, olivopontocerebellar atrophy is a specific disease process. It is not a congenital, but a degenerative, hereditary and familial disease. As the cases of Arndt, Dejerine and Thomas, Spiller [36] (case 4), Cassirer [37] and others show, it may also occur sporadically. It belongs with the class of heredodegenerative diseases, such as Friedreich's ataxia, Huntington's chorea, familial forms of spastic paraplegia and other conditions. It may be classified as a systemic disease in which certain groups of ganglion cells become affected, just as certain groups of ganglion cells are affected in amyotrophic lateral sclerosis, bulbar paralysis and progressive muscular atrophy. The cell groups affected in olivopontocerebellar atrophy are comprised of the ganglion cells of the olivary bodies, the arcuate nuclei and the basal (ventral) portion of the pons. Essick [38] demonstrated the common origin of the foregoing ganglion cell groups. From his brilliant studies he came to the conclusion that they all come from the lip of the rhomboid fossa, the rhombic lip being their "common ancestor." From the rhombic lip the ganglion cells migrate as neuroblasts to the pons, through a restricted pathway called by Essick the corpus pontobulbare. In figure 8 a part of the latter is situated over the restiform body, which it overlaps, and histologically consists of multipolar ganglion cells and a network resembling the nuclear masses of the pons. The same may be said of the arcuate nuclei, which, "including a part of the olive," are formed by ganglion cells migrating from the rhombic lip over the ventral surface of the medulla. With Bakker,[39] Winkler and others, one may thus consider olivopontocerebellar atrophy an abiotrophy of the cell bands of Essick. The condition of the ganglion cells of the pontobulbar body in our case could not be ascertained, as the specimen was stained by the method of Pal and Kultschitzky.

As has been pointed out, olivopontocerebellar atrophy may be incomplete, just as amyotrophic lateral sclerosis may be incomplete, occurring

36. Spiller, W. G.: Four Cases of Cerebellar Disease (One Autopsy) with Reference to Cerebellar Hereditary Ataxia, Brain **19**:588; 1896, Case 4.

37. Cassirer, R., in Lewandowsky, M. H.: Handbuch der Neurologie, Berlin, Julius Springer, 1912, vol. 3, p. 874.

38. Essick, Charles: The Corpus Ponto-Bulbare: A Hitherto Undescribed Nuclear Mass in the Human Brain, Am. J. Anat. **7**:119, 1907; The Development of the Nuclei Pontis, the Nucleus Arcuatus in Man, ibid. **13**:55, 1912.

39. Bakker, S. P.: Atrophia olivo-ponto-cerebellaris, Ztschr. f. d. ges. Neurol. u. Psychiat. **89**:213, 1924.

as bulbar paralysis or progressive muscular atrophy.[40] Olivopontocerebellar atrophy, for instance, may manifest itself mainly as a lesion of the basal nuclei of the pons or olivary bodies, giving origin to pontocerebellar and olivocerebellar types of atrophy. In Messing's case the atrophy was mainly pontocerebellar, as the olives were involved only slightly and partially. In the cases of Holmes, Hänel and Bielschowsky and Schob,[41] the second case of Barker and probably the cases of Adolf Meyer and Schroeder and Kirschbaum [42] and Kufs,[11] the atrophy was olivocerebellar. Hänel and Bielschowsky even once suggested pontocerebellar and olivocerebellar types of atrophy, but they finally preferred to group them with the anomalous forms of heredocerebellar ataxia. On the other hand, Bakker considered olivocerebellar atrophy a prestage of the olivopontocerebellar type, which, in his opinion, would have developed had the patient lived longer. Of interest is also the fact that of the four cases on which Marie, Foix and Alajouanine based their classification of the cerebellar atrophy which they named "late cerebellar, predominantly cortical," in at least three there was some atrophy of the olives and of the olivocerebellar nerve fibers. Some of their pictures (figs. 11 and 12) [2] resemble closely figure 5 and especially figure 6 of our series.

As to the changes in the spinal cord, they are those of combined degeneration of the posterolateral tracts, as seen in Friedreich's ataxia. They have nothing to do with the degeneration of Essick's cell bands, which, as has been emphasized, is the anatomic base of a definite pathologic entity—olivopontocerebellar atrophy. Clinically, this type of cerebellar atrophy also is represented by a definite syndrome, the heredocerebellar ataxia of Marie. Of the two names by which one disease process has thus been designated (one for the clinical, the other for the pathologic features), the better known name given it by Marie should be retained, just as the name of Friedreich is retained for a kindred clinical condition (Friedreich's ataxia). Marie's and Friedreich's ataxias may be combined and are usually familial and hereditary. In both, the ataxia and other signs and symptoms are due not to the involvement of the cerebellum itself but to that of the cerebellar connections originating in the pons (pontocerebellar) or medulla (olivocerebellar)

40. Hassin, G. B.: Degenerative Erkrankungen mit besonderer Bevorzugung motorischer Leitungsbahnen und Kerne und kombinierte Systemerkrankungen, Monatschr. f. Psychiat. u. Neurol. **86**:255 (Sept.) 1933.

41. Schob, F.: Weitere Beiträge zur Kenntnis der Friedreich-ähnlichen Krankheitsbilder, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:188, 1921.

42. Schroeder, A., and Kirschbaum, W.: Ueber eigenartige degenerative Erkrankungen des Zentralnervensystems mit vorwiegender Beteiligung des olivocerebellaren Systems und Grosshirnrindenveränderungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:681, 1928.

in Marie's type and to that of the spinocerebellar connections in Friedreich's type. The distribution and type of the lesions in Friedreich's ataxia resemble the degenerative characteristics present in subacute combined degeneration of the cord, strange as such a view expressed elsewhere [43] may appear to some overcritical but sterile minds.

CONCLUSIONS

1. Olivopontocerebellar atrophy of Dejerine and Thomas is a definite pathologic entity, differing from sclerotic or crossed atrophies of the cerebellum.

2. Clinically, it is similar to heredocerebellar ataxia of Pierre Marie.

3. It is a disease of the so-called cell bands of Essick, the homologs of the gray matter of the medullary olives and the arcuate and pontile nuclei.

4. The atrophy of the cerebellum is secondary to that of the white fibers emanating from the cell masses of Essick.

5. The atrophied and sclerosed cerebellar white substance causes retrograde ("transsynaptic") degeneration of the Purkinje and other cells of the cerebellar cortex.

6. Aside from typical or complete forms of olivopontocerebellar atrophy there are also atypical, incomplete or even rudimentary types, in which only the pons or only the olivary bodies are involved.

7. In the classification of cerebellar atrophies by Marie, Foix and Alajouanine groups 2 (familial atrophy) and 3 (the large group of acquired cerebellar atrophy) may be combined in one group, comprising the most common and probably the only types of cerebellar atrophy—olivopontocerebellar, sclerotic and crossed.

DISCUSSION

Dr. La Salle Archambault, Albany: The histologic changes so well described by Drs. Hassin and Harris are strictly analogous to the changes described by André Thomas in his thesis, "Observations Four and Five," in which he created the type referred to by the authors under the name of olivopontocerebellar atrophy. These changes were subsequently also found in a case reported by Dejerine and André Thomas. In 1918, in a paper that I devoted to the study of parenchymatous atrophy of the cerebellum, I took the liberty of incorporating the salient clinical features and the striking histologic changes in this very interesting form of degenerative atrophy of the cerebellum and its related pontobulbar nuclear masses and fiber pathways. To me it seems impossible to admit the statement of Dr. Hassin and Dr. Harris that the "foregoing changes must be considered as the pathologic basis of what Marie described as heredocerebellar ataxia," or else that the latter condition "is the same as olivopontocerebellar atrophy of Dejerine and Thomas."

43. Hassin, G. B.: Histopathology of the Peripheral and Central Nervous Systems, Baltimore, William Wood & Company, 1933, p. 95.

I am well aware that there always has been and still is in the old world a strong tendency to individualize syndromes and create new entities, whereas in the new world the opposite urge to generalize and homologize is quite as developed. To my mind, both trends are equally hazardous. I need only recall (the authors have already done so) that Marie fought valiantly for the autonomy of heredocerebellar ataxia, which he regarded on both clinical and anatomic grounds as entirely distinct from Friedreich's disease or hereditary ataxia, and it is known now that even in France this distinction is no longer held by competent neurologists.

But when it comes to assimilating Marie's hereditary cerebellar ataxia into Dejerine and Thomas' olivopontocerebellar atrophy, I think that it is time to utter a word of caution. It is impossible for me to admit that such outstanding contemporary masters of French neurology as Pierre Marie, André Thomas and Dejerine were describing under different names a complex of clinical signs and histologic changes that Drs. Hassin and Harris are now trying to say are identical. I grant that these syndromes are closely related.

Dr. Adolph Meyer, Baltimore: This is another of those interesting families with symptom complexes and signs which in the eyes of some have to be gathered together into one entity and in the eyes and thought of others are divided according to particular data. It so happens that not much is known of the differentiation of symptoms due to cerebellar involvement. There are certain broad features of ataxia with which all are familiar, but when I look at the different anatomic conditions and also look over the history of the development I have the impression that there are great structural differences, and I cannot help feeling that there are also functional differences. There are instances in which the symptoms are much more of the type seen in cases of cerebellar ataxia. In other instances symptoms are somewhat more of the type seen in ataxia due to lesions of the afferent system or of the segmental-cerebellar connections, and then there can be disorders of the type of which Drs. Hassin and Harris have given an example; such conditions are apparently quite different, because in them one is dealing not with the segmentocerebral apparatus but with the cerebrocerebellar apparatus. Disturbances of this type are to my mind essentially different from the condition in one of those cases of Sanger Brown's that I described about thirty years ago. There were, to my surprise, remarkably few changes in the cerebellum. The cerebellum also was quite different from that in the case which I am going to mention. It seemed to be involved by ramification of the disease very much more than intrinsically. Involvement was by way of systems that go from the cerebral parts toward the cerebellum. I have a case, the report of which is not published as yet because of certain unclear features, in which the condition also belongs to the cerebellar disorders. It is a case in which there is a uniform absence of the Purkinje cells and in which there is no evidence of any degeneration of the pons. I am not aware of any particular involvement of the segmentocerebellar afferent system. But it is a case which to all intents and purposes is striking because of its positive features, a more choreiform reaction, which in cerebellar conditions is not present in its, one might say, aggressive form. After all, cerebellar disorders seem to be rather more elaboration disorders and not initiators of disturbance, at any rate in this fundamental differentiation. This is one of the situations which make it appear regrettable that the term pathology is still used only for anatomic data. Such usage justifies the separation of study by the clinician, who does not see the autopsy material and has to make his examinations in the dark, from study by the autopsy worker, who has not seen the clinical facts. It is to be regretted that it is not recognized that there is a pathology which applies to the patient as well as to autopsy material. As soon as one considers pathology in that sense and leaves the clinical and autopsy

study in the hands of the same investigator, one can recognize that there is a general group of cases that show a "cerebellar symptom complex;" but one ought to go further. Just as in the domain of polyneuritis efforts are being made to secure clinical differentiations that are more significant and more likely to throw light on different structural distributions, so in this field I think it is perhaps better if, stimulated by experience with different structural involvements, one recognizes that there are probably also differentiations in the cerebellar symptom complex, according participation to more than one type, in this case the thalamo-olivary and pontile systems, that is to say, in the forward connections, while in those older cases of Londe and others that are largely cases of involvement of the segmentocerebellar afferent system there are probably also functional differences. Just one term should not be applied to these cases too quickly.

Dr. George B. Hassin, Chicago: I wish to assure Dr. Archambault that I admire the work of Marie and Dejerine probably even more than he does. I think I paid the greatest compliment to Pierre Marie by proving that the clinical entity he described actually exists, and it is surely not my fault that the ten members of a family who exhibited a typical picture of heredocerebellar ataxia also exhibited an equally typical pathologic picture of olivopontocerebellar atrophy.

What other interpretation can one give to these cases? Deny that they were those of olivopontocerebellar atrophy or say that the pathologic study was wrong? Neither Dr. Archambault nor any one else would do that, for the facts presented can easily be affirmed. Marie himself never studied a case of heredocerebellar ataxia, which he described on the basis of the reports by others (Menzel, Nonne, Sanger Brown, Klippel and Durante) and the pathologic basis of which was not understood. It proved to be what, seven years later, was described by Dejerine and Thomas as olivopontocerebellar atrophy, but neither Marie nor other investigators knew it to be a pathologic entity.

This investigation is a research study of a rare condition, covered probably more thoroughly than other similar cases. Even Winkler's case, a report of which was published two years ago, is not so complete, as it has been studied mainly from the anatomic point of view. Mathieu and Bertrand suggested that heredocerebellar ataxia and olivopontocerebellar atrophy possess common features, at least at certain levels of the central nervous system. This has been emphasized in the present paper. Probably the French authors did not care to be more outspoken and to consider the two conditions one disease process.

I appreciate much the discussion and suggestions of Dr. Meyer, but I wish to emphasize one point, that no matter how many ganglion cells are destroyed in the cerebellum clinical signs or symptoms will not be exhibited unless the connections between the cerebellum and the spinal cord, or between the cerebellum and the pons, or between the cerebellum and the medulla are affected. Whether the spinocerebellar, the pontocerebellar or the olivocerebellar tracts are involved, whether outside or within the cerebellum, the lesion results in so-called cerebellar symptoms (ataxia, disturbances of speech and coordination) with which the cerebellum itself has nothing to do. The involvement of the foregoing links thus may lead to a picture either of Friedreich's or of Marie's ataxia, which one may call heredocerebellar, but these two morbid conditions are not one disease process.

SURGICAL PATHOLOGY OF SUBDURAL HEMATOMA

BASED ON A STUDY OF ONE HUNDRED AND FIVE CASES

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In 1934 one of us [1] reviewed a series of sixty-two cases of subdural hematoma and advanced the theory that the so-called chronic hematoma is only a late stage of an unrecognized earlier acute form. It was furthermore pointed out that so far as those data went there was evidence to show that every subdural hematoma starts as a mixture of blood and cerebrospinal fluid imprisoned in a space from which diffusion cannot readily take place. This mixture develops into a completely solid clot, at the one extreme, or a collection of fluid with a high protein content, at the other. The intermediate clots which possess any significant degree of fluidity were held to be expanding lesions. This was believed to be due to the osmotic effect of two fundamental factors: the dissolution of the blood and the diffusion of fluid across the pia-arachnoid, which acts as a dialyzing membrane. The dissolution of blood causes a high protein content of the solution and the diffusion of fluid, an increasing volume of solution. With the increase in the number of cases available for study from sixty-two to one hundred and five it has been possible to show that in all fundamentals these claims hold true.

Pathologically, subdural hematomas are of three types, which merge into one another and vary in their development as time goes on, depending on the original relationship between the solid and the fluid constituents. Regardless of type, however, each tumor begins as the immediate response to the rupture of a vessel into the cranial subdural space. This is undoubtedly frequently accompanied by a varying degree of associated leakage of cerebrospinal fluid from the subarachnoid space, which must occur through a temporarily open tear in the arachnoid. This syndrome follows most frequently a blow on the head, which may be either severe or trivial. It may be associated also with a variety of diseases, the most important of which are those that affect the integrity of the cerebral vascular system. In this report only cases of hematoma resulting from trauma are included.

From the Neurosurgical and Neurological service of the Boston City Hospital and the Department of Neurology of the Harvard Medical School.

1. Munro, Donald: The Diagnosis and Treatment of Subdural Hematomata: Report of Sixty-Two Cases, New England J. Med. **210**:1145 (May 31) 1934.

SOLID HEMATOMA

The first type of hematoma is that in which only blood is deposited in the subdural space. This is the classic form. Its organization, as seen in specimens removed at autopsy, has been well described and studied by Putnam [2] and Leary.[3] This takes place from the periphery toward the center. If the organization is rapid and efficient and if the clot is not too thick, the entire hematoma will eventually become solid and may remain so for years, in rare cases even becoming calcified (fig. 1). If the organization is less efficient, the center of the clot may remain partially liquefied as a result of local necrosis. None of the solid clots absorb cerebrospinal fluid, however, because

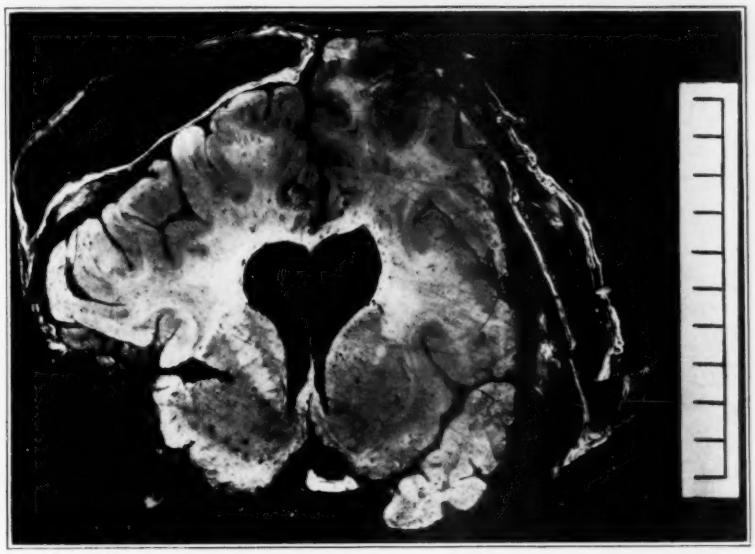

Fig. 1.—Calcified bilateral subdural hematomas showing evidence of more recent additional hemorrhages. These were removed at autopsy from a woman aged 29 who had had institutional care as a mentally defective, epileptic patient, since she first entered school as a child. Pulmonary tuberculosis was also present. The data on this case were made available by Dr. Anna Allen.

when the fluid portion is present it is separated from the arachnoid and the subarachnoid space. The hematoma is therefore a fixed, non-expansible lesion except in those rare instances in which repeated hemorrhages take place within the original clot.

2. Putnam, T. J., and Cushing, H.: Chronic Subdural Hematoma, Arch. Surg. **11**:329 (Sept.) 1925.

3. Leary, Timothy: Subdural Hemorrhages, J. A. M. A. **103**:897 (Sept. 22) 1934.

The histologic changes in the solid part, as measured by a microscopic study of the dura and the limiting membranes of the clot, are remarkably constant and can be accepted as an approximate measure of the age of the clot. Although the accuracy of this estimation decreases as the end of the period is approached, the changes can be made to serve as a time table. Against this table the changes in clots removed either surgically or at autopsy the age of which cannot be determined by the patient's history can be checked. A group of forty-seven such specimens of known ages, varying from a few hours to two years, form the foundation on which the data to be detailed are based.

In the solid hematoma the successive histologic changes result, as pointed out by Leary,[3] from the inadequate efforts of the dura to remove the clotted blood. The first step in this process is a laying down of fibrin around the edge of the blood clot and its invasion by fibroblasts. This starts at the surface of the clot next to the dura. The pia-arachnoid plays no part, and the surface of the hematoma adjacent to it is organized by extension from the dura. Since these fibroblasts grow only from the dura, the membrane on the dural side of the clot (outer membrane) is of fairly uniform thickness at any given stage of development. The membrane on the inner surface of the clot (inner membrane), however, varies considerably in thickness. At the margins of the clot it is approximately equal in thickness to the outer membrane but it becomes progressively thinner as it recedes toward the center. The growth of fibroblasts from the inner and the outer membrane until they meet to form a compact tissue may completely organize a small hematoma. In such cases the blood is gradually liquefied and carried away by histiocytes without the formation of any free fluid. In a larger clot, however, liquefaction of a large portion usually occurs before organization is completed.

From Two to Twenty-Four Hours After Injury.—The earliest change is caused by the deposition of fibrin around the edge of the clot. The connective tissue of the dura is stimulated and fibroblasts grow from it into the underlying clot. Specimens from six such hematomas were examined. In all the specimens the blood appeared to be fresh. The red cells and leukocytes were well preserved. On the outer surface of the clot there was a thin layer of fibrin (fig. 2).

From Thirty-Six Hours to Four Days After Injury.—A few fibroblasts may appear at the junction of the dura and the clot as early as thirty-six hours after the hemorrhage. These fibroblasts increase in number, and by the fourth day there is a definite layer, three or four cells in thickness, beneath the dura. Five specimens are included in this group. One removed thirty-six hours after injury showed a few fibroblasts at the junction of the dura and the clot. The blood retained its fresh appearance, however. One removed four days after injury showed definite evidence of the formation of a membrane. Beneath the dura there was a layer of young fibroblasts two or three cells in thickness. The red blood cells in the underlying clot had begun to lose their sharp contour and stained rather poorly.

From Five to Eight Days After Injury.—With each succeeding day there is an increase in the thickness of the layer of fibroblasts, so that by the eighth day a definite neomembrane is visible. Seven such clots were available. In each of them there was a definite neomembrane under the dura, with extension of fibroblasts into the underlying clot. There was a slight progressive increase in the thickness of the membrane daily until on the eighth day there was a neomembrane from twelve to fourteen fibroblastic nuclei in thickness. The blood in the specimens

Fig. 2.—Section of a blood clot removed from the subdural space two days after injury to the head. The blood is fairly well preserved. A layer of fibrin can be seen on the surface of the clot. In figures 2 to 7 *C* indicates clot; *D*, dura; *F*, fibrin; *IM*, inner membranes; *LF*, layer of fibroblasts; *N*, neomembrane, and *OM*, outer membrane.

removed seven or eight days after injury appeared old and was becoming liquefied, especially in the lower portion of the clot. Pigment-containing histiocytes were seen in all specimens removed after the fifth day. Figure 3 shows a section of a clot removed five days after injury. At that time the dura is especially rich in

fibroblastic nuclei, which appear to be growing down toward the clot and forming a layer at the margin between these two structures. Figure 4 shows a well formed neomembrane beneath the dura seven days after injury.

Eleven Days After Injury.—We have only one specimen which was removed between the ninth and the twelfth day. This was removed eleven days after injury. No section of the dura was included in the specimen. The blood in the clot, which was fairly large, was almost completely liquefied and was broken up into

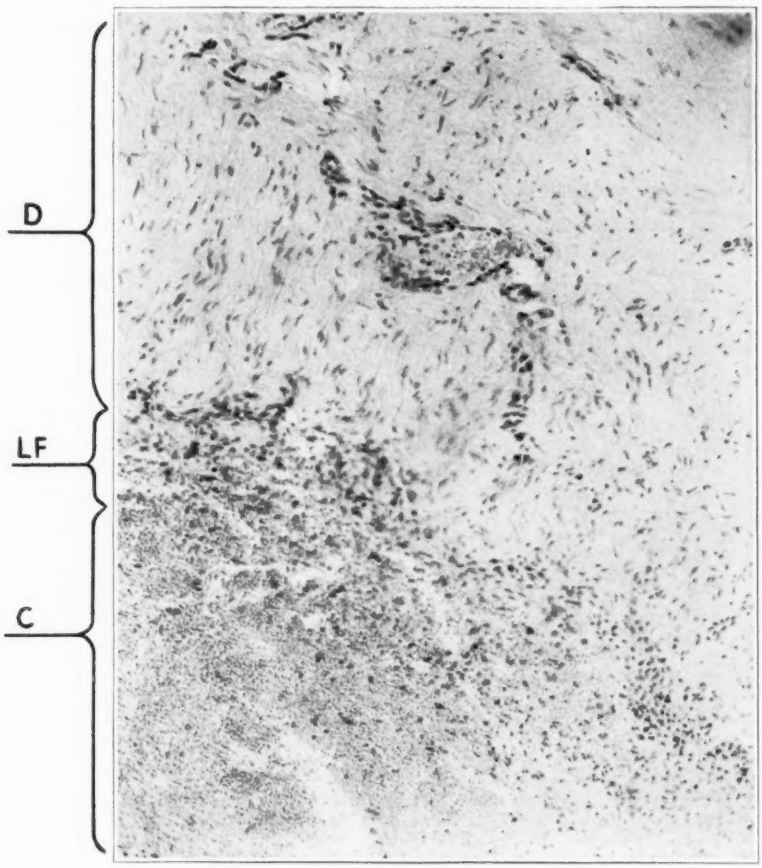

Fig. 3.—Section of the dura and the underlying clot removed five days after an injury to the head. There is an increase of fibroblastic nuclei in the dura, and a layer of fibroblasts can be seen between the dura and the clot.

islands by thick strands of fibroblasts. This liquefaction may be continuous during the first three weeks after injury, particularly in the central and lower portions of the hematoma. Concomitantly there is an increase in the thickness of the neomembrane attached to the dura, and pigment-laden phagocytes appear in the lower portions of the membrane. Strands of fibroblasts invade the clot, splitting it into islands.

From Thirteen to Seventeen Days After Injury.—By from the fifteenth to the seventeenth day a definite membrane may be found on the inner surface of the clot (inner membrane), with fibroblastic strands extending inward from it. There were twelve specimens in this group. In the large clots islands of liquefied blood were present in the sections, but in the smaller ones the blood was almost entirely absorbed, being limited in the latter instance to a few scattered red blood cells and many pigment-laden phagocytes. The thickness of the neomembrane varied from

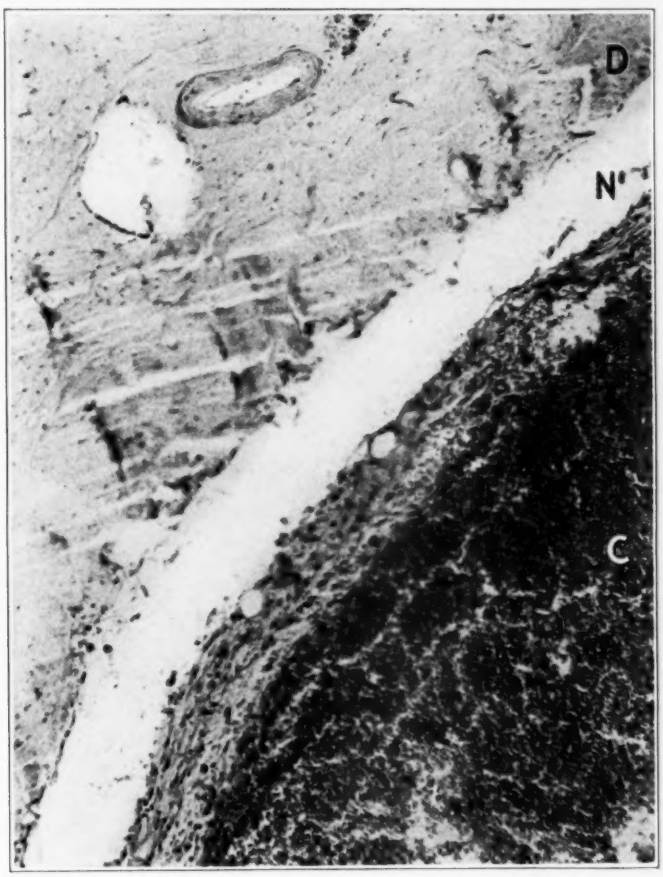

Fig. 4.—Section of the dura and a clot removed seven days after an injury to the head. A well formed neomembrane is visible between the dura and the clot.

one-third to one and one-half times that of the attached dura. Variation in the thickness of the outer membrane in different portions of the section was noted in several instances. A definite inner membrane was present in two specimens, removed on the fifteenth and the seventeenth day, respectively, the blood clots being small and almost completely absorbed. Even there, however, a thin layer of blood remained between the outer and the inner membrane, the inner one being only a few fibroblastic nuclei in thickness.

From eighteen to Twenty-Six Days After Injury.—Only one specimen (on the twentieth day) was removed between the eighteenth and the twenty-sixth day. Sections showed well formed inner and outer membranes. The outer membrane was approximately equal in thickness to the dura, the inner membrane being only about half as thick. The intervening blood was so liquefied that it did not fix. Numerous pigment-containing phagocytic cells were scattered throughout both membranes.

From Twenty-Seven to Thirty-Six Days After Injury.—In the six specimens removed during that period there were well formed membranes. In those originating as small hemorrhages the blood had been almost entirely absorbed and replaced by a compact neomembrane, in the substance of which a few red blood cells and

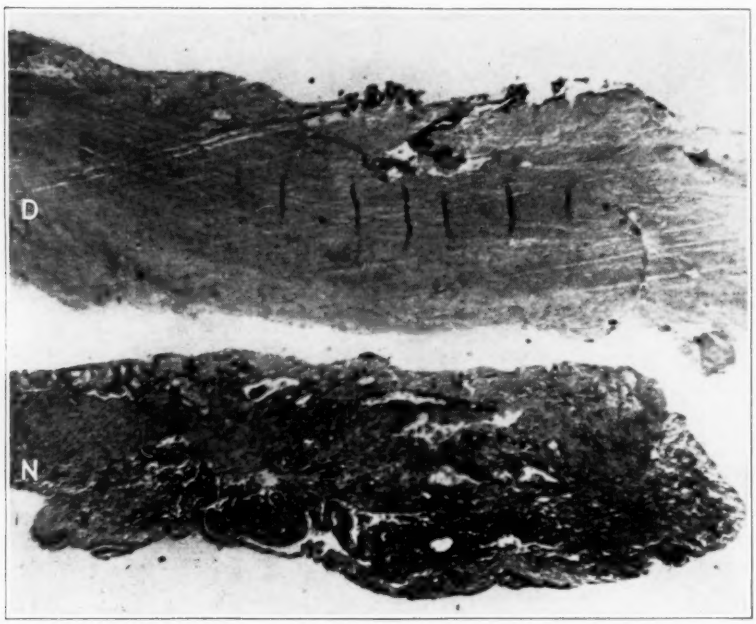

Fig. 5.—Section of the dura and the underlying neomembrane removed one month after an injury to the head.

many pigment-laden phagocytic cells were scattered. When the hemorrhage had been larger, however, liquefied and disintegrated blood was contained between the inner and the outer membrane. A section from a clot removed one month after injury (fig. 5) showed the dura with a loosely woven neomembrane beneath it, the blood having been almost completely absorbed.

The changes that occur in the following months are chiefly a more thorough organization of the clot, with removal of all the free blood. The number of fibroblastic nuclei decreases, and they are replaced by a hyalin-like connective tissue, so that after a year the neomembrane closely resembles the dura.

From Thirty-Seven to Ninety-Three Days After Injury.—Four specimens removed between the thirty-seventh and the ninety-third day after injury were available. One removed forty-one days after onset showed well formed inner and outer membranes containing a small amount of blood which had not been

completely organized. Two others, ninety days old, showed in section a thick hyalin-like membrane beneath the dura. No separation between the inner and the outer membrane was evident, though a few red blood cells and pigment-containing phagocytes were scattered throughout both structures. In the fourth case there was a thick neomembrane enclosing a mass of disintegrated blood (fig. 6).

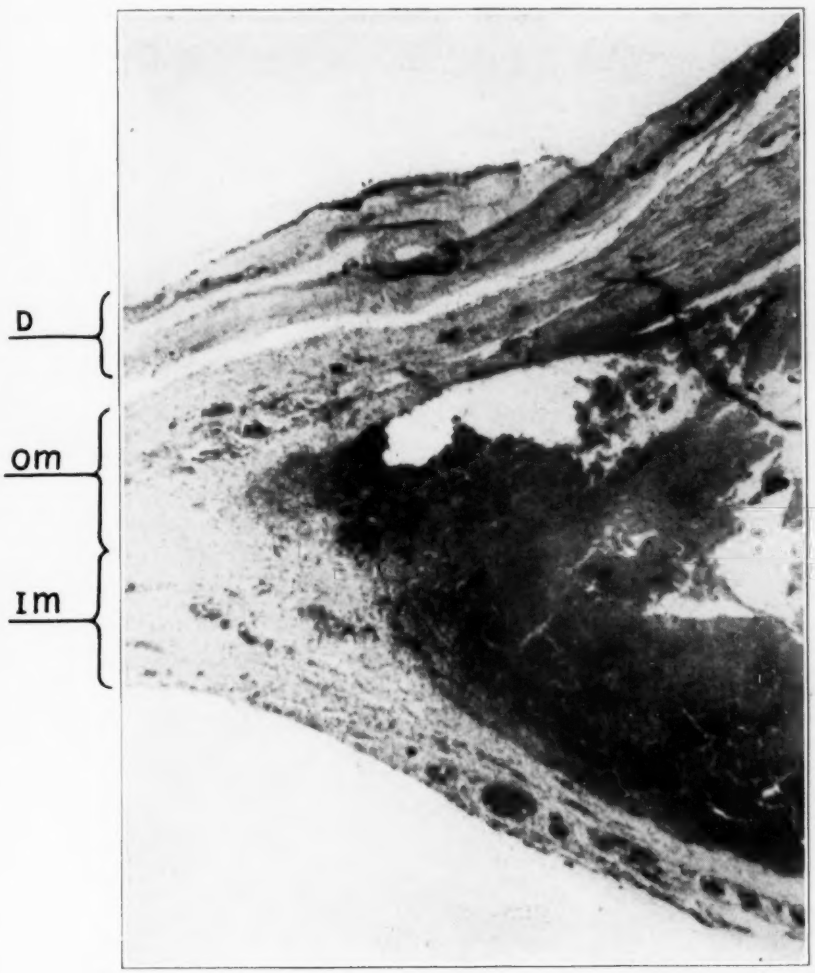

Fig. 6.—Section of the dura, an underlying hematoma and the neomembrane removed three months after an injury to the head. This section was taken from the margin of the clot and shows the inner and outer membranes surrounding a very large clot.

From Six Months to One Year After Injury.—One specimen examined at six months showed a thick, fibrous neomembrane from which all blood had disappeared except for a few isolated pigment-containing phagocytes.

From One to Two Years After Injury.—Three specimens were removed more than one year after the injury (two after two years and one after one year).

Each showed a membrane lying beneath the dura which, histologically, was almost indistinguishable from it. This membrane was composed of hyalinized connective tissue with very few fibroblastic nuclei. Differentiation was possible only because

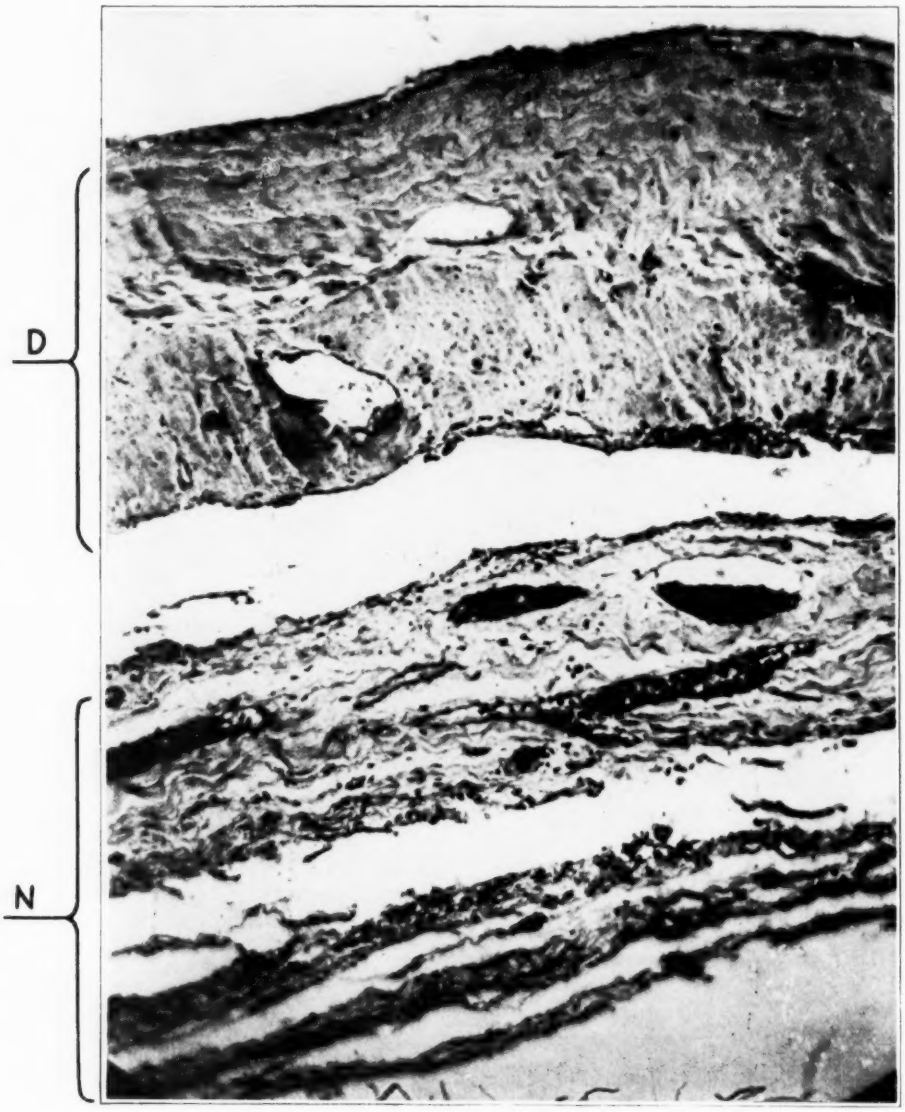

Fig. 7.—Section of the dura and the underlying neomembrane removed one year after an injury to the head.

all the fibers were parallel. Sections from the specimen removed one year after injury contained, in addition, pigment-laden phagocytes. Figure 7 shows the neomembrane one year after the injury.

The formation of large blood spaces, which Leary [3] described as sinusoidal vessels, is said to be peculiar to the histologic picture of subdural hematoma. These are known in the literature as "giant capillaries." Examples were noted in the neomembranes in a number of our specimens removed between the twentieth and the ninetieth day after the hemorrhage. Leary [3] stated that the dilatation of these vessels is due to back pressure, which in turn results from the imperfect venous drainage of the membrane. In addition, it has been postulated by many writers that these vessels frequently rupture and cause a further extravasation of blood. We were able to demonstrate evidence of such secondary hemorrhage in one of our cases. In all the others, however, the free blood appeared to be of the same age in all sections taken from the same hematoma.

MIXED HEMATOMA

The second type is the mixed hematoma. This starts as a varying amount of gross blood or clots mixed with greater or less amounts of cerebrospinal fluid and all contained within the subdural space. A certain number of these specimens will offer for study not only an organizing clot attached to the dura but also associated free fluid for chemical analysis. Microscopic study of the organization of the smaller clots checked against the time table referred to previously will give not only the age of the clot but also and of necessity the age of the associated fluid. The age of the fluid can be expressed in approximate terms of the protein content. These data are presented in the form of a graph the ordinates of which give the number of milligrams of protein per hundred cubic centimeters of fluid and the abscissas, the lapse of time in days, months or years. This will help one to visualize the progressive changes that occur in the fluid part (fig. 8).

The shape of the first limb of the graph demonstrates a constant addition of protein to the solution in question. This is enclosed in the subdural space, which has no vascular connection. It is inconceivable, therefore, that this constantly increasing protein can come from any source other than the blood which was deposited a short time previously between the dura and the arachnoid. This dissolved blood, a solution composed chiefly of sodium chloride and proteinates, will ultimately become completely free from solid clots. Because of the high percentage of protein molecules therein and in spite of the easy diffusibility of the contained chloride ions, the osmotic pressure of this fluid as compared with that of the spinal fluid or the blood is relatively high and is constantly increasing. The end of this period of solution or the peak of the graph falls at about the sixteenth day. This corresponds with reasonable accuracy to the end of the period which is required to dissolve the red blood cells in the subarachnoid space.[4] The descending limb of the graph, on the other hand, is of such shape as to be best explained by predicating a process of dilution. This takes place rapidly at first and then

4. Merritt, H. Houston, and Fremont-Smith, F.: The Cerebro-Spinal Fluid, in Nelson Loose-Leaf Living Medicine, New York, Thomas Nelson & Sons, 1932, vol. 6, chap. 26, p. 551.

more slowly, the diminution in the rate of dilution being progressively more marked as the percentage of the protein in solution grows less. In conformity with the results of Gardner's [5] experiments, we believe that this dilution comes from the addition of fluid and chiefly through the breakdown of the protein molecules into a greater number of smaller molecules, which are amino-acids and other end-products. This tends to lower the osmotic pressure of the subdural fluid toward the level of that of the diluting fluid. If it is assumed that the arachnoid acts as a dialyzing membrane and that fluid passes through it from the cerebrospinal fluid toward the solution with a higher osmotic pressure, one has a tenable explanation of the known facts, i. e., an increase in the amount of fluid in

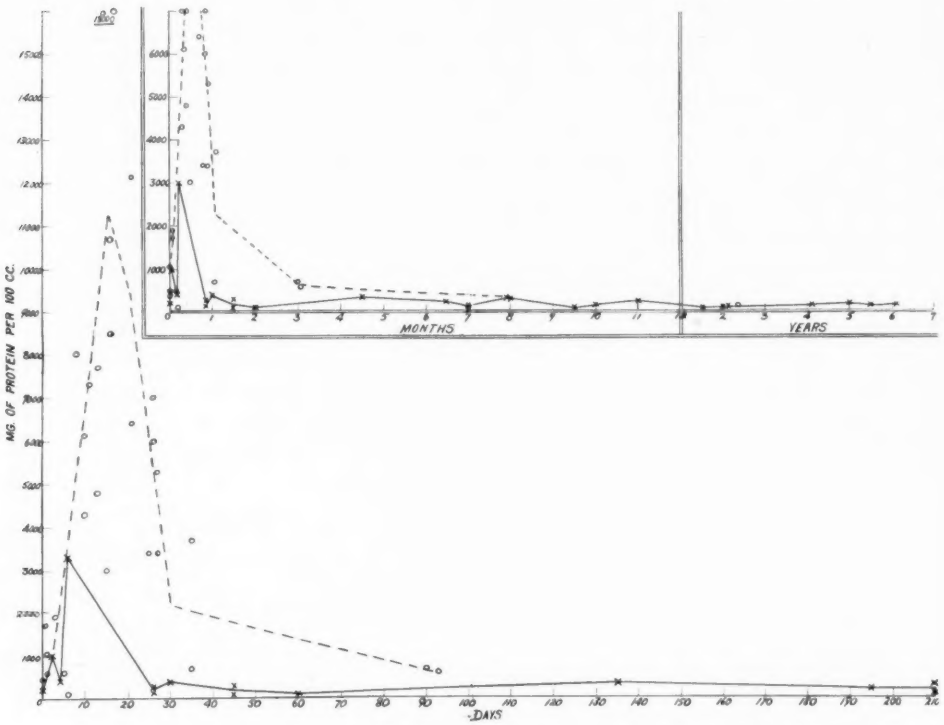

Fig. 8.—Graphs showing the changes in the protein content of subdural hematomas. The circles represent the protein content of thirty fluid hematomas with gross clots. Twenty of these were verified histologically. The crosses represent the protein content of twenty-six fluid hematomas which contained blood but no gross clots. None of these were verified histologically.

the hematoma as well as a decrease in the concentration of protein. Furthermore, there is a physicochemical process [6] in action which would produce just such a

5. Gardner, W. J.: Traumatic Subdural Hematoma, with Particular Reference to the Latent Interval, Arch. Neurol. & Psychiat. **27**:847 (April) 1932.

6. Lewis, W. C.: Donnan's Theory of Membrane Equilibria, in Lewis, W. C. M.: A System of Physical Chemistry, New York, Longmans, Green & Co., 1923, vol. 2, p. 309.

graph as has resulted from the study and arrangement of the data collected from this series of cases. It can be predicted further that this process should reach an end-point of dilution and a resultant flattening out of the graph at some point at which the protein content will be less than 200 mg. per hundred cubic centimeters. This will be due partly to the production of osmotic equilibrium through a shift of chloride ions across the membrane and partly to the decrease in the protein content. Dilution as well as the splitting up of the larger protein molecules into the smaller and more diffusible constituents characteristic of protein end-products accounts for the decrease in protein. Since the exact degree of permeability of the dialyzing membrane is an important factor which is undeterminable, only approximations can be reached. The graph presented herewith (fig. 8), however, conforms with the proposed explanation. The rise is rapid and sustained. The fall is at first rapid and then succeeded by a period of gradual slowing, which in turn is followed by a flat section that, as will be pointed out, extends over a period of years. During the final phase the solution should be clear, with a yellowish tinge; it is free in the subdural space and varies in amount in different cases, though in each case it remains at a constant volume; it contains a percentage of protein definitely higher than that of the cerebrospinal fluid. In brief, then, it is possible to show that blood mixed with fluid, which is assumed to be cerebrospinal fluid, and incarcerated in the subdural space dissolves in an average period of sixteen days. Thus, a solution with a constantly increasing protein content is produced. Thereafter a rapid process of dilution takes place for the two succeeding weeks, after which a still slower dilution occurs for at least two months. The ratio of the percentage of protein in the fluid hematoma during the second two weeks to that during the three succeeding like periods is 9 : 4, and to that during the final period, 9 to 3. The protein content of the solution at the end of that time is too low to be of significance in influencing the exchange of fluid.

Such a succession of events characterizes the formation and development of the second type of, or mixed, subdural hematoma. In conjunction with this it is possible to check the approximate accuracy of the figures that go to make up the graph. As suggested, this is done by studying the time element in relation to the protein content of the fluid part of the hematoma and checked against the histologic aspect of the associated clots. This makes it possible to reduce to two choices the approximate age of an unknown subdural fluid. This is determined by noting the protein content of the fluid and finding its position on the chart. This determination may be especially valuable in the case of a patient about whom for a variety of reasons the history is absent, untrustworthy or deliberately falsified.

FLUID HEMATOMA

The third type of subdural hematoma is completely fluid and contains no grossly solid clots of any sort. These hematomas present two varieties. There is the fresh subdural collection in which a minimum amount of blood is added at the time of injury to a maximum amount of cerebrospinal fluid. There is also the old residual fluid from which the

original clots completely dissolve during the interval between the receipt of the injury and the removal of the fluid. These have formerly been indiscriminately spoken of as hygromas.[7] Obviously their time-protein content relationship is not subject to such histologic confirmation as may be applied to the mixed hematomas. Careful checking of the date of injury together with the shape of the graph leads us to believe, however, that our data are reliable.

There were twenty-six of these fluid hematomas. The seven examined within thirty days of injury were held to be fresh, while the sixteen falling within a period extending for from four and a half months to seven years after injury were considered as old solutions. The remaining specimens might fall into either group. When grouped to form a graph, in accordance with the method already described, the curve is flatter than the previous one. This is in conformity with the fact that less blood had been mixed with more cerebrospinal fluid. However, the fundamental shapes remain the same and follow the requirements postulated in the preceding section. The steep rise associated with the solution of the blood is present but reaches a peak on the sixth as opposed to the sixteenth day. This, again, is followed by a descent, which is rapid at first and then slows up as the dilution is carried to the point at which the protein concentration has been brought down into the low levels. There, however, the rapid phase of dilution is completed in only three weeks at the rate of 800 mg. per hundred cubic centimeters every five days, and the low point is in the neighborhood of 200 mg. These sections include the data on all the fresh fluids. From there to over seven years the graph is essentially flat, what variations there are being within the limits of accurate observation. Sixteen analyses provide the material for the latter section; they were all of old fluids. Eight were made in the last eight months of the first year following injury and the others at intervals of from eighteen months to seven years. The average protein content of the first eight was 194 mg. while that of the last was 119 mg. The fluid was found only by exploratory craniotomy. From 50 to 100 cc. was easily collected at operation from beneath either the temporal or the frontal lobe or both. This was in turn followed by profuse watery drainage from the wound for the first two days after operation. As it is impossible to tell from the evidence how much blood originally went into solution, it is as reasonable to consider these fluids as the end-results of mixed hematomas as of solutions that had no gross blood in them at any time. It is furthermore certain that these amounts of fluid cannot be classed as a normal content of the subdural space, as an artefact produced at operation or as material which escaped through an unrecognized artificial opening into the subarachnoid space.

COMMENT

In making the accompanying graphs it became evident that the figures in a few cases fell so far outside the curves as to be worthy of special investigation. Two of the specimens contained clots which had been independently examined, as well as fluid in which the protein had been measured. The protein values were such that they might be placed on

7. Naffziger, H. C.: Subdural Fluid Accumulations Following Head Injury, J. A. M. A. **82**:1751 (May 31) 1924.

either the rise or the fall of the graph. There was no available history as to the time of the injury in either case. Histologic study placed the protein figures properly and dated the injury about ten days earlier than it had been thought to occur. As both were potentially cases of criminal assault this was not without importance. Six other cases in which the protein values did not conform were not included in the study: four because there was no reliable historical or histologic confirmation and the other two because the estimations of protein were known to be only roughly approximate. Separate hematomas from both sides of the head were examined six times. One in particular is interesting in that the history, which before operation was believed not to be significant, showed two separate injuries one year apart. Fluid removed from each side of the head at separate operations within a week of each other, however, gave protein contents which showed an approximate difference of a year in the positions on the graph.

Determinations of protein were made by the method of Denis and Ayer as described by Ayer, Dailey and Fremont-Smith.[8] Because at operation there was of necessity a contamination of the subdural fluid by fresh blood, specimens that were collected for examination were sent at once to the laboratory. They were centrifugated at high speed (usually within five minutes of their collection) after a part had been reserved for a blood count. The determination of protein was done on the supernatant fluid, and a red cell count was made on the reserved uncentrifugated specimen. Eight-tenths gram of protein per thousand erythrocytes, as counted in the reserved specimen, was then subtracted from that figure as a correction for the serum protein added to the fluid with the fresh blood.[9] However, it was only an approximate correction, as there is no accurate measure of the protein added through hemolysis of the new cells. Because of that and because of the high dilution needed for a quantitative determination on the fluids with a very high protein content, the final figures for protein also are only approximate.

The accuracy of the histologic examination also is limited, as it is obvious that the exact age of a clot after complete organization is unpredictable. On the other hand, for the first month after injury variations are demonstrable every few days. From then until the complete organization the changes become progressively less marked, and the estimation of the age becomes progressively less accurate. Even with

8. Ayer, J. B.; Dailey, M. E., and Fremont-Smith, F.: Denis-Ayer Method for the Quantitative Estimation of Protein in the Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **26**:1038 (Nov.) 1931.

9. Solomon, P.; Dailey, M. E., and Fremont-Smith, F.: Contamination of the Cerebrospinal Fluid by Blood, Arch. Neurol. & Psychiat. **31**:1222 (June) 1934.

these admitted approximations, however, the importance of the study of the surgical pathologic picture of a subdural hematoma as a potential check on the accuracy of the history of injury should not be overlooked. This might prove to be particularly important when criminal legal action or recovery of damages under an insurance policy might ensue.

Most important of all perhaps is the evidence here presented that a subdural hematoma is, in part at least, so constituted as to remain unabsorbed in a nonencysted fluid form for a number of years. This is an abnormal intracranial condition and one that need not produce local or localizing signs of cerebral damage. It is reasonable to suppose that it is associated with some type of symptomatology, however, and we believe that this particular type is included among that great group of conditions labeled posttraumatic state or neurosis and associated with injuries to the head.

CONCLUSIONS

An analysis of figures obtained by a chemical and histologic study of a group of one hundred and five subdural hematomas is presented.

Subdural hematomas can be divided into three groups.

The first group, or solid subdural hematomas, with rare exceptions are not expanding lesions; they may remain unrecognized for years and can be accurately placed as to age up to from two or four months.

The second group are mixed, solid and fluid subdural hematomas and are expanding lesions for three months, after which they remain constant in size. The increase in size and the decrease in the protein content occur coincidentally with the division of the large protein molecules into the smaller ones of the end-products of protein destruction and by virtue of the addition of fluid from the cerebrospinal fluid by dialysis through the arachnoid. They may remain unrecognized for years; they produce symptoms that conform to those produced by posttraumatic neurosis and can be accurately placed as to age up to four months by a study of the protein content of the fluid portion.

The third group are fluid subdural hematomas. In the early stages they are slowly expanding lesions up to one month, as determined by the same method as that used for the second group, and from then on they remain unchanged in size. They may remain unrecognized until found at exploratory craniotomy. They may cause symptoms identical with those of the late stages of the second group and, except by consideration of the history, can be accurately placed as to age only during their first three weeks of existence. Fluid removed at a later date may have its origin, as far as the available evidence shows, in either the earliest stages of a fluid hematoma or the late stages of a mixed hematoma.

The conception of the solid chronic subdural hematoma as an entity should be abandoned, and the lesion should be recognized as only one form of the late stages of a previously undiagnosed acute process.

VASOMOTOR PHENOMENA ALLIED TO RAYNAUD'S SYNDROME

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Since the publication in 1882 of Raynaud's [1] original description entitled "Observations on Local Asphyxia and Symmetrical Gangrene" there have been numerous factors reported as causal in this syndrome. Regardless of the etiology, Raynaud knew that the condition which he described was more prevalent in nervous women, a fact obtaining today and suggesting cortical or subcortical influence.

We propose to show that local asphyxia or abnormal vasoconstriction resulting in syndromes analogous to that of Raynaud may develop from stimuli arising at any level from the cerebral cortex down to the peripheral vessels themselves.

REPORT OF CASES

CASE 1.—F. W., a girl, aged 15, entered the University Hospital on Sept. 16, 1928, with the chief complaint of "difficulty in seeing." The mother stated that after the age of 12 this child had not developed physically as had her other child. The girl had never menstruated. The intellect had always been normal. For the past year and a half marked polyuria had been present with excessive thirst and nocturia from three to four times. This had entirely disappeared four weeks previous to her entrance into the hospital. About eight weeks before admission, projectile vomiting had appeared, and she began to complain of visual disturbance. Increasing drowsiness was noted, the child falling asleep almost anywhere. Headache was not present, though it had been noted for a period some months previously.

Visual fields taken at this time at the Battle Creek Sanitarium revealed increasing diminution in the lower segments, with red-green color blindness. The fundi were normal; the sella turcica was normal. The basal metabolic rate at this time was —18. She was referred to this clinic by Dr. W. H. Riley, with a diagnosis of suprasellar tumor.

Examination.—The patient was well nourished but underdeveloped; she was well oriented but somewhat dull. There was complete absence of pubic and axillary hair. The heart and lungs revealed no abnormalities. The blood pressure was 80 systolic and 55 diastolic, the pulse rate 100 and the white blood cell count 10,000.

From the Department of Surgery, University of Michigan Medical School.

1. Raynaud, M.: Local Asphyxia and Symmetrical Gangrene of the Extremities, translated by Thomas Barlow in Selected Monographs, London, New Sydenham Society, 1888.

The pupils were somewhat dilated but reacted to light and in accommodation. There was an alternating strabismus of 7 degrees, with some difficulty in convergence. The right optic disk showed a forward bulging of about 1.5 diopter; the left, less than 1 diopter. Both disks were pale and somewhat waxy in character. The visual fields could not be charted. The remaining cranial nerves revealed no abnormality. The tendon reflexes were equal but somewhat overactive. The abdominal reflexes were obtained. The normal response to plantar stimulation was obtained on both sides. No cerebellar signs were demonstrated. A roentgenographic examination of the head showed digital markings over the entire skull, but no evidence of pathologic change in or about the sella turcica.

Course.—In the succeeding days the mental state became poorer until September 22, when she became practically comatose and the temperature rose to 101 F. rectally. There was slight rigidity of the neck but no Kernig sign. On the following day the patient was unconscious and uttered an occasional meningitic cry. At noon the right arm was cyanosed. At 5 p. m. the cyanosis had disappeared, and the left foot and lower part of the leg presented the cyanosis typical of advanced Raynaud's disease. The leg was cold, and a drop of perspiration was seen in each hair follicle. A colored drawing was made at this time. Two hours later the right leg presented a similar cyanosis. Lumbar puncture at this time revealed colorless clear fluid containing 53 cells per cubic millimeter. There was normal reduction of Fehling's solution. The Nonne-Apelt reaction showed no ring in phase 1 and slight opalescence in phase 2. The Kahn reaction was negative; the colloidal gold curve was 1123321000; the mastic curve, 244221.

On the following morning the cyanosis, with no edema, was still present in both legs. Respirations ceased at 9:28 a. m.

Autopsy.—In the region of the optic chiasm was a slight swelling; the tuber cinereum was bulging out ventrally. On section a tumor was seen extending from the posterior perforated space to the optic chiasm anteriorly, running up along the lower borders of the third ventricle and involving the interventricular nucleus of the hypothalamus. The mass pressed out on the optic tracts. It was not encapsulated. The ventricles were undilated and contained clear fluid (fig. 1).

Microscopic examination revealed the tumor to be a large alveolar round cell sarcoma (fig. 2). This diagnosis was confirmed by Dr. Percival Bailey.

Comment.—In this case there was a definite pathologic lesion in the hypothalamus, a region considered by most anatomists and physiologists as the autonomic center. Bucy [2] has aptly stated: "Within the hypothalamus is a mechanism which functions as the central ganglion of the sympathetic nervous system." There was a history of earlier diabetes insipidus, more recent disturbance of the sleep mechanism and finally Raynaud's syndrome, commencing first in one arm, then disappearing to recur in the leg of the opposite side and finally involving both legs. The unilateral appearance and the sequence of events definitely rule out circulatory failure as the cause of the cyanosis, while the observations at autopsy clearly indicate that the vasomotor disturbance was of central origin.

2. Bucy, P. C.: Vasomotor Changes Associated with Paralysis of Cerebral Origin, Arch. Neurol. & Psychiat. **33**:30 (Jan.) 1935.

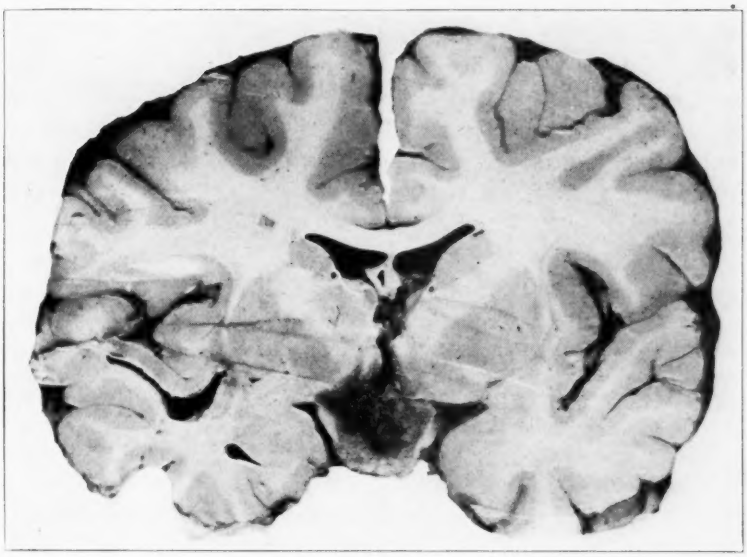

Fig. 1 (case 1).—Tumor of the hypothalamus.

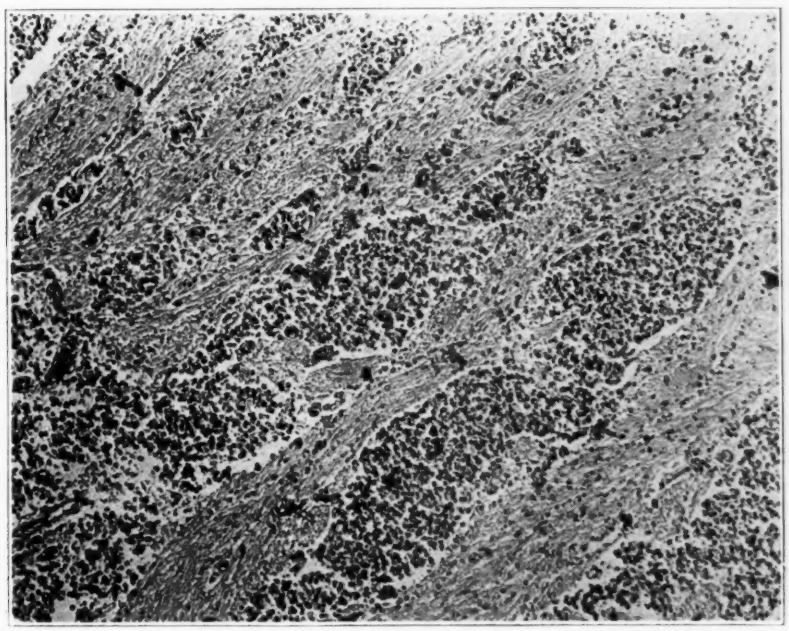

Fig. 2 (case 1).—Photomicrograph of the tumor of the hypothalamus.

Penfield [3] also described a cerebral tumor producing symptoms of apparent autonomic origin under the term "diencephalic autonomic epilepsy." Attacks would occur in which there was dilatation of the pupils, with bulging of the eyeballs, flushing of the face and arms, lacrimation, profuse sweating and rapid heart beat. The tumor lay at a higher level than in our case, being in the anterior part of the third ventricle and pressing on the mesial anterior and superior aspects of both thalami.

CASE 2.—E. H., a man, an American, a protestant, aged 28, entered the University Hospital with the chief complaint of painful, swollen feet. Three months previously, during the course of an acute respiratory infection, he awakened one morning with marked pain, redness and swelling in the right foot. Four days after the acute onset he had chills and sweats on four successive nights. The foot became swollen, cold and blue. The swelling persisted for two months and then diminished. Both feet then were almost continuously cold and sweating, with occasional attacks of burning in the right foot. He was entirely incapacitated for work and walked on crutches.

Examination.—The patient appeared well nourished, fairly intelligent and not acutely ill. General examination gave entirely negative results except in the extremities. Neurologic examination gave negative results.

Both upper and lower extremities were cold and clammy. There was no cyanosis of the upper extremities. The right foot was bluish red, cold and perspiring. There was no marked blanching on elevation. There was a fairly sharply demarcated color change in the midleg from the normal to cyanosis. The anterior tibial artery pulsated strongly; the posterior tibial artery was poorly felt. When dependent the leg soon became painful. The left leg presented a similar change in color, though not nearly so marked. It did not become painful when dependent. The color in both legs blanched readily on pressure. With the leg in the horizontal position the cyanosis became much less marked.

The urine and the blood were normal; a Kahn reaction was negative. The basal metabolic rate was plus 1. Roentgenographic studies of the right foot and tibia demonstrated "multiple punched-out areas of rarefaction of the tarsal bones and lower end of the tibia. This gives the appearance of an atrophic condition following circulatory disturbance."

Operation.—Following spinal anesthesia there was a marked rise in the temperature of both legs. Abdominal sympathectomy was performed by one of us (M. M. P.) on Oct. 10, 1930. The right sympathetic chain was divided just over the brim of the pelvis. The dissection was carried upward to the second lumbar vertebra; three ganglia were excised, one of which was evidently the fusion of two ganglia. On the left a similar procedure was carried out, four ganglia being identified.

Course.—Convalescence was uneventful. The legs became warm and ceased to sweat immediately after the operation. The patient was discharged on the sixteenth day with complete freedom from symptoms. A later report stated that the legs were entirely symptom-free but that the hands became cyanosed on exposure to cold.

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3. Penfield, W.: Diencephalic Autonomic Epilepsy, Arch. Neurol. & Psychiat. **22**:358 (Aug.) 1929.

Microscopic Examination.—The ganglia were examined by Dr. Albert Kuntz,[4] who stated that there was marked leukocytic infiltration as well as some increase in stroma. He also reported that the ganglion cells were in general in fair condition, though the chromic substance was somewhat meager. There were relatively few cells which appeared pale and exhausted, though some showed beginning neuronophagia. He stated: "The entire picture seems to me to be one of some degree of inflammation and overactivity on the part of the ganglion cells."

Comment.—Case 2 is, of course, not typical of Raynaud's disease as ordinarily described. Regardless of the name applied, there has been a constant deleterious vasoconstrictive element, as evidenced by the beneficial effect of cutting off the abnormal impulses by sympathectomy. The later history of cyanosis of the hands on exposure to cold makes it more nearly Raynaud's syndrome. The pathologic changes in the ganglia suggest that the primary cause of the vasomotor phenomena lay there, acting as a constant irritant with resulting sympathetic stimulation.

An interesting case was reported by Bennett and Poulton [5] in a man aged 66. "In April 1922 he began to experience pain in his fingers and this had become steadily worse until we saw him July 17, 1927. The color of the fingers was slaty blue, quite typical of Raynaud's. The pain in the fingers was continuous but increased in paroxysms." He was operated on, the right inferior cervical sympathetic ganglion being excised without difficulty. Death occurred a few minutes later when periarterial sympathectomy was being performed on the brachial artery. Autopsy revealed a large carcinoma of the lesser curvature of the stomach, 4 inches (10.16 cm.) in diameter. Examination of the right inferior cervical ganglion removed at operation revealed carcinomatous metastases infiltrating normal sympathetic ganglion cells. The only other metastases in the body were in a few lymph nodes. No mention is made of the left ganglion.

CASE 3.—B. Z., a Polish girl, aged 12, entered the University Hospital on April 9, 1930, with a history of pain in the right hip and difficulty in walking. She had been well until two months before, when she fell on the ice. Three weeks following this the pain started. It was noted that she was not steady on her feet and that it was necessary to swing one foot across the other in walking. Increasing blueness of the hands and feet had arisen since the onset of this illness. No sphincteric disturbance had been noted.

Examination.—The patient was well developed. The gait was slow and not spastic, but typical of a bilateral, almost complete paralysis of the extensor system. The pupils were equal and regular and reacted to light and in accommodation. There was no nystagmus, and there were no cranial nerve palsies. Biceps and triceps jerks were present but slightly diminished. The abdominal reflexes were active in all four quadrants. The knee and achilles jerks were not

4. Kuntz, Albert: Personal communication.

5. Bennett, T. I., and Poulton, E. P.: Raynaud's Disease Associated with Cancer of the Stomach, Am. J. M. Sc. **176**:657 (Nov.) 1928.

obtained. Plantar irritation caused no movement of the toes. Vibratory sense was preserved in both ankles; deep tendon sensibility and sense of position of the toes were normal. There was hypesthesia in the region of the fourth and fifth sacral segments, which was more pronounced on the left.

The most striking part of the picture was the marked vasomotor disturbance. Both hands, when dependent, became markedly cyanotic. The cyanosis somewhat slowly disappeared on elevation. The chest and upper part of the back were flushed and felt abnormally warm. The skin of the abdomen felt cool as compared with that of the chest.

There was no localized atrophy of the lower extremities. The feet and legs in the sitting position were so cyanosed as to be almost the color of slate. No edema was present. On pressure over the cyanosed area with the thumb the cyanosis disappeared, leaving a red area corresponding to the thumb pressure standing out sharply for at least five minutes before resuming its bluish hue. On elevating the foot the cyanosis gradually disappeared.

Lumbar puncture revealed a complete block, with xanthochromic fluid. Kahn tests of the blood and spinal fluid were negative.

Diagnosis.—Dr. Carl Camp made a diagnosis of tumor of the cauda equina, with possible extension upward, giving pressure on the intermediolateral columns and resulting vasomotor disturbance.

Operation.—Under avertin anesthesia the first to the fourth lumbar laminae were exposed by one of us (E. A. K.). On removing the third lamina it was thought that the dura had been opened, as there was an escape of a considerable amount of clear fluid which came from what was apparently a very thin dura adherent to the lamina. The epidural fat was entirely absent over this area but was seen in normal amount beneath the fourth lamina. On stripping the epidural fat beneath the fourth lamina it was seen that what had been apparently dura was a cyst lying on the dura itself with a blind end just beneath the upper part of the fourth lumbar lamina. The cyst stripped easily from the underlying dura. It extended laterally just anterior to the transverse diameter of the vertebral canal on both sides. It was seen to extend upward beneath the twelfth dorsal lamina. On exerting traction the upper blind end was easily released. It had extended to approximately the ninth dorsal lamina. Following the removal of the cyst the vertebral canal was seen to be abnormally wide.

Microscopic Diagnosis.—The pathologist reported that the material was folded dense connective tissue membrane having the histologic structure of both dura and meninges—a meningocele.

Course.—On the day following operation the feet felt warmer. A few days later, when the legs were placed in a dependent position the cyanosis took longer to appear and was not of the same intensity. The hands showed even more improvement. Twelve days after the operation the patient was able to stand. The feet became cyanosed, the hands only slightly so. Strength in the lower extremities rapidly improved, with return of the reflexes.

The patient returned to the clinic about four and a half months after the operation. Gait was then normal. The upper and lower extremities showed no abnormality in color.

Comment.—In this case there was a definite lesion of the spinal cord with advanced vasomotor changes, apparently a combination of abnormal vasoconstriction and vasodilatation. Just how the hands became involved in such a lesion can only be conjectured, but there are various possi-

bilities, the most intriguing of which is that cell bodies in the lowest dorsal intermediolateral columns may send their white rami up the ganglionic chain to the cervicodorsal region. It is possible that this is a case of reflex vasoconstriction, the term "reflex" here denoting nervous influence acting from a distance on blood vessels.

In discussing the rôle played by the cerebral cortex in the causation of vasomotor phenomena we can cite little experimental evidence. Kennard,[6] working in Fulton's laboratory on the effect of removing the premotor cortex of monkeys and chimpanzees, showed that the skin of the affected extremities becomes colder than that of the normal side. These differences in temperature may reach as high as 4 F. Langworthy and Richter [7] on stimulating certain areas of the cortex of cats produced a galvanic skin response, but this is a measure of sweat gland rather than vasomotor activity.

The clinical evidence is more abundant.

CASE 4.—D. C., a boy, aged 13, was admitted to the University Hospital in a comatose condition three days after a coasting accident in which he had sustained a severe injury to the head. The home physician stated that the patient's condition had been satisfactory until the night before admittance to the hospital when he "took a change for the worse, the color becoming ashen."

Examination.—On admittance to the ward at 10:15 a. m. the boy was dehydrated and apparently in grave condition. The rectal temperature was 100.6 F., the pulse rate 124 and the respiration rate 24.

An extensive compound depressed fracture, later shown by portable x-ray film, was palpated in the left parietal region. The optic fundi were normal. A central type of facial paralysis was demonstrated on the right on pressure over the supra-orbital ridges. There was right hemiparesis, with increased reflexes. Babinski's sign was bilaterally present.

The exceptional feature of the case was a symmetrical cyanosis (fig. 3) which anteriorly extended from the face down almost to the inguinal folds, and posteriorly, over the entire back and buttocks. It extended lower on the right thigh, as can be seen in the postmortem photograph (fig. 4). Below the cyanosed area, and sharply demarcated from it, the skin was completely blanched. The dorsalis pedis artery was not definitely palpated on either foot. Within fifteen minutes the blanching had ascended anteriorly almost an inch (2.5 cm.), as shown by the dotted lines on the premortal photograph. There was no difference in blood pressure in the left arm and leg.

Course.—Five per cent dextrose was given intravenously. The blood pressure soon rose to 120 systolic and 80 diastolic. At 11:45, respiration ceased, though the pulse continued. Oxygen was forced, and a lumbar puncture was done. The fluid was grossly clear but under considerable pressure.

Operation.—The patient was taken to the operating room under forced oxygen and an operation performed without anesthesia. A large area of bone over the

6. Kennard, M. A.: Vasomotor Representation in the Cerebral Cortex, Science **79**:348 (April 13) 1934.

7. Langworthy, O. R., and Richter, C. P.: The Influence of Efferent Cerebral Pathways upon the Sympathetic Nervous System, Brain **53**:178, 1930.

site of fracture was rongeured away. There was a small amount of extradural clot. The dura was under great pressure and showed a small tear, through which contused, nonpulsating brain was herniating. The dura was opened widely for decompressive purposes.

Fig. 3 (case 4).—Ascent of ischemia. The lower dotted line shows the original level.

Fig. 4 (case 4).—Photograph taken two and a half hours post mortem, showing intensification of the cyanosis from hypostasis.

On completion of the operation 0.5 cc. of a 1:1,000 solution of epinephrine was given intravenously. The heart responded immediately with an increased rate and forcefulness, and the area of cyanosis assumed an erythematous hue. The patient was now placed in a Drinker respirator. The cyanosis soon reappeared, and death occurred a few minutes later.

Autopsy.—This was performed two and a half hours after the patient's death. The cyanosed area was still present and was intensified over the back by hypostasis. There was no evidence of trauma to the trunk. The brain, which weighed 1,540 Gm., was swollen, edematous and markedly anemic. The convolutions were flattened. A definite pressure cone was present. There was a contrecoup contusion of the right frontal lobe. Besides the operative defect, many smaller old hemorrhages were present throughout the hemispheres. The hypothalamic area and brain stem were essentially normal except for anemia.

Comment.—The brain was so extensively involved that little can be gathered from the point of view of localization, though the hemispheres suffered far more than the rest of the brain. What did occur was abnormal vasoconstriction over an extensive area in no way corresponding to a segmental distribution. The cyanosis described was probably due to the patient's poor general condition. The pallor that was creeping upward was undoubtedly vasoconstriction due to central stimulation or inhibition acting on lower centers.

GENERAL COMMENT

Bucy [2] observed a woman, aged 45, who, following a vascular accident undoubtedly in the left internal capsule, showed complete disappearance of the right brachial and radial pulses. There was feeble pulsation in the right axillary and temporal arteries, with moderate pulsation in the right carotid artery compared with strong pulsation in all the arteries of the left side. The blood pressure in the right arm was unobtainable in all but one determination for three days, while the blood pressure in the left arm was always within the limits of normal. The right arm and toes were cyanotic and cold at first. The patient recovered completely.

Zenner and Kramer [8] reported the case of a man, aged 57, with a meningioma apparently in the left frontoparietal region. During an attempt at removal the radial pulse disappeared from the right wrist while remaining of good quality in the left wrist. Three days later the tumor was removed, and during this procedure the phenomenon recurred. On the following day the two pulses were equal. No record of the blood pressure was made.

Osler [9] stated that some of the "worst cases" appear in hysterical persons. It is not uncommon to enter the room of one of these patients suddenly and see a typical attack appear. This in itself suggests a cortical or subcortical origin or influence. Such a case is mentioned by Fox,[10] that of a woman who frequently experienced paroxysms of local

8. Zenner, P., and Kramer, S. P.: Operation for Brain Tumor, with the Hitherto Unrecognized Circulation Phenomena, New York M. J. **90**:651, 1909.

9. Osler, W., and McCrae, T.: Modern Medicine, Philadelphia, Lea & Febiger, 1928, vol. 5, p. 723.

10. Fox, C.: On Two Cases of Raynaud's Disease, Tr. Clin. Soc. London **18**:300, 1884-1885.

asphyxia. He stated that "her extremities go blue 'in a second' if she is startled by any knock on the door or unusual occurrence."

Clymer [11] mentioned a case in which "a traveling mountebank exhibited a wonderful control over the hue of his face, becoming flushed or deadly pale as he pleased." He mentioned another case of a "gentleman who for seventeen years had been able to produce at will contracture and roughness of the skin with prominence of the papillae and erection of the hairs—cutis anserina or gooseflesh—with apparent loss of heat and visible paleness of the surface." This certainly suggests voluntary sympathetic control.

Maxwell [12] studied a young man who could voluntarily erect the hairs and produce cutis anserina. The vasomotor changes occuring at the time of the voluntary erection of the hair were studied with the finger plethysmograph. Invariably the erection of the papules was accompanied by a reduction in the volume of the fingers. One might say that this patient could produce voluntary vasoconstriction.

Whitfield [13] said: "It is not uncommon for very nervous patients to suffer from so-called 'dead finger' and to state that this condition may be brought on by their being startled. Within the last few years I have had such a patient and while questioning her I contrived to upset a heavy tray of notes onto the floor so as to make a sudden and considerable noise. In a short time three of her fingers, two on the left hand and one on the right, slowly became ivory white."

Angell and Thompson,[14] working with the plethysmograph on normal persons, found that all emotional states, agreeable or disagreeable, produced vasoconstriction. One can imagine how much more striking this would appear in a case of Raynaud's syndrome. Shepard,[15] also working with the plethysmograph, found that the only factor which gave vasodilatation was attention to the member in the plethysmograph. Recent work at the University of Michigan by Coller and Maddock [16] shows the marked effect of the emotions on the temperature of the skin. The temperature of the skin has been taken with the patient resting

11. Clymer, M.: Lectures on the Palsies and Kindred Disorders of the Nervous System, M. Rec. **5**:145 (May 16) 1870.

12. Maxwell, S. S.: A Case of Voluntary Erection of the Human Hair and Production of Cutis Anserina, Am. J. Physiol. **7**:369 (July 1) 1902.

13. Whitfield, A.: Some Points in the Etiology of Skin Diseases, Lancet **2**:168 (July 23) 1921.

14. Angell, J. R., and Thompson, H. B.: Organic Processes and Consciousness, Psychol. Rev. **6**:32, 1899.

15. Shepard, J. E.: Organic Changes and Feeling, Am. J. Psychol. **17**:522, 1906.

16. Coller, F. A., and Maddock, W. G.: Personal communication.

quietly in bed. A discussion causing an emotional reaction on the part of the patient has immediately resulted in a drop in the temperature of the toes. Camp [17] described an interesting case in a woman, aged 33, seen by him in January 1914 because of inability to walk. Typical astasia-abasia was present. During the winter of 1911-1912 blanching of the third fingers had come on in attacks, followed by redness, swelling and "some pain." This had gradually grown worse until all the fingers and toes became involved in the attacks, which occurred at room temperature, the hands becoming "purple and mottled." Psychotherapy was commenced merely to relieve the hysterical paraplegia. After a few days the patient suddenly arose from her wheel chair and walked 3 miles (about 5 kilometers) down the street. A report in September 1914 stated that she had experienced no further attacks of circulatory disturbance.

The field of hypnosis offers considerable evidence in favor of induced vasomotor control. Under suggestion blisters have been formed and needles passed through extremities with no bleeding.

Weir Mitchell [18] mentioned a case of unilateral edema on the paralyzed side in a hysterical patient. Pricking with a pin during the stage of edema produced no bleeding.

Hysteria closely parallels self-induced hypnosis. The pathology of hysteria has escaped all present-day methods. Most autopsies in typical cases of Raynaud's disease have shown no pathologic changes which may be considered as causal. We think, therefore, that some typical cases of Raynaud's disease, which we know frequently occur in hysterical persons or in those who are prone to hysteria, may have the same pathogenesis as the hysteria. Whether this pathogenesis is purely psychic or whether there is an ultramicroscopic or chemical change remains for the future to tell.

The rôle played by the blood vessels alone in the causation of Raynaud's syndrome is difficult to evaluate. The procedure of sympathectomy and ganglionectomy, as worked out by Adson and Brown,[19] has cured Raynaud's disease in most cases. This certainly suggests that the etiologic factor must be on the central side of the ganglia or in the ganglia. Recent work by Lewis [20] has thrown doubt on this view.

17. Camp, Carl: Personal communication.

18. Mitchell, Weir: Unilateral Swelling of Hysterical Hemiplegia, Am. J. M. Sc. **88**:94 (July) 1884.

19. Adson, A. W., and Brown, G. E.: Physiologic Effects of Thoracic and of Lumbar Sympathetic Ganglionectomy or Section of the Trunk, Arch. Neurol. & Psychiat. **22**:322 (Aug.) 1929.

20. Lewis, T., and Landis, E. M.: Some Physiological Effects of Sympathetic Ganglionectomy in the Human Being and Its Effect in a Case of Raynaud's Malady, Heart **15**:151, 1930.

He believed that he was blocking all sympathetic fibers to certain portions of the hand by local anesthesia, and yet he still obtained cyanosis. He [21] ascribed the beneficial effect of sympathectomy to cutting out additional stimuli coming to the affected blood vessels from higher centers.

We recently did a bilateral cervicodorsal and abdominal sympathectomy in a typical case of Raynaud's disease in a woman aged 23. There has never been any trouble with the feet since. Both hands, however, still become cyanosed, though she is otherwise symptomatically free. Horner's syndrome is present bilaterally. There has never been any sweating in arm, hand or leg, although the abdomen sweats profusely at times.

An anesthetic was injected locally to block the ulnar and median nerves at the right wrist. After immersion of the hands in cold water cyanosis gradually developed and was equal in the two hands. We cannot help but think that here the vessels are at fault, if not primarily, at least at present. Had there been a regeneration of sympathetic fibers or some remaining fibers there should have been some diminution of the cyanosis in at least one finger after the injection of the anesthetic.

Might there be a humoral factor, such as Cannon's sympathin, acting etiologically in Raynaud's syndrome? We think not because, though sympathectomy usually relieves the disease syndrome, it does not remove the source of sympathin; moreover, the terminal blood vessels still exist to be acted on by any humeral factor.

It is probable that in some cases of Raynaud's syndrome the smooth muscle of the smaller vessels has an abnormal irritability. It is well known that the heart, though having a double nervous mechanism, can still contract when freed from this controlling factor. We see no reason why vessels with a smooth muscle of abnormal irritability might not be prevented from giving a pathologic response by eliminating an additional vasocontrictive factor through sympathectomy.

Most smooth muscle, as well as cardiac muscle, contracts rhythmically when severed from its nerve supply, as shown by Gaskell,[22] Alvarez [23] and Lake.[24]

In Tigerstedt's [25] "Physiologie des Kreislaufes" a number of experiments are cited in which a rhythmic contraction of isolated arterial strips

21. Lewis, T.: Personal communication.

22. Gaskell, W. H.: On the Innervation of the Heart, with Especial Reference to the Heart of the Tortoise, J. Physiol. **4**:43, 1883.

23. Alvarez, W. C.: The Mechanics of the Digestive Tract, New York, Paul B. Hoeber, Inc., 1922.

24. Lake, N. C.: Observations upon the Growth of Tissues in Vitro Relating to the Origin of the Heart Beat, J. Physiol. **50**:364 (Sept.) 1916.

25. Tigerstedt, R.: Die Physiologie des Kreislaufes, ed. 2, Berlin, W. de Gruyter & Co., 1922, vol. 3, p. 51.

was obtained. It seems possible that later work may demonstrate an abnormal contractability in strips of artery taken from persons with advanced Raynaud's disease, especially those whose condition was not relieved by sympathectomy.

SUMMARY

A series of cases demonstrating abnormal vasomotor phenomena has been presented. The excitor area in the first case lies in the hypothalamus, in others in the spinal cord and sympathetic ganglia, while in the last case it might be in the peripheral vessels. It is thought that some typical cases of so-called Raynaud's disease may be caused by the same factor which underlies hysteria.

In conclusion, we believe that Raynaud's disease is merely a syndrome since it could be caused by an exciting factor located in the cerebral cortex, the various nervous pathways and even the peripheral vessels themselves.

A TECHNIC OF INJECTION INTO THE GASSERIAN GANGLION UNDER ROENTGENOGRAPHIC CONTROL

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The modern operation of section of the posterior root of the fifth cranial nerve for trigeminal neuralgia is one of the greatest achievements of surgery. There are series of hundreds of cases on record with a mortality of less than 1 per cent. The operation has become so standardized and so satisfactory that, in the United States at least, few attempts have been made to find any substitute for it. It has, however, certain undeniable disadvantages. In the first place, the mortality can be kept low only by a certain degree of selection of cases. In the second place, section of the root is a major operation entailing discomfort and a period of disability, which should not be taken lightly. In the third place, the results of operation cannot be predicted in cases which are at all atypical, and many a surgeon is haunted by one or more "gasserian ghosts" who complain bitterly of the annoyance of a numb face in addition to the original pain.

As an alternative to operation, injections of alcohol are often resorted to—either peripherally, into the second and third branches of the trigeminal nerve, or else into the ganglion itself. These treatments have the advantage that they entail a relatively short period of disability and the disadvantages that both of them are excessively painful and uncertain. Even the most experienced operators encounter a tangible proportion of failures and find patients disinclined toward a second attempt. Injection into the peripheral portions of the nerve has the further disadvantage of giving only temporary relief but the advantage of absolute safety. The anesthesia afforded by intraganglionic injection is permanent, but if it is incomplete the same possibility of recurrence exists as in subtotal section of the root.

The question of the relative safety of intraganglionic injection as compared with section of the root is much discussed. In neurosurgical clinics in America the idea appears to be widespread that injection into the ganglion is distinctly more dangerous than the usual operation; in

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England and Europe exactly the opposite attitude is often held. A survey of the literature shows that a great many hundreds of injections have been carried out by such experts as Harris [1] and Härtel [2] without a single death but that occasional fatalities have occurred in smaller series in less skilled hands.[3] The mortality even then is probably far lower than that of section of the root in the hands of the inexpert.

It appeared to us, therefore, that if some modification of the technic of intraganglionic injection could be devised which would enable it to be carried out under anesthesia and with roentgenologic control, so as to increase the accuracy, it might prove to be preferable to either of the present procedures. A somewhat similar method has been employed by Zenker [4] and by Stiasny,[5] but it is not clear whether they have used roentgenologic control in precisely this manner during the course of the injection.

Of the three possible routes through the foramen ovale to the ganglion, that described by Härtel appeared to be the most suitable for the purpose. N-methylcyclohexenyl-methylmalonylurea,[6] a new anesthetic for intravenous injection, was chosen as it has the advantages of safety and of prompt and brief action. The procedure was practiced on the cadaver, and an attempt was made to carry it out under the fluoroscope, but this proved impracticable. The routine procedure that was finally evolved is as follows:

TECHNIC

The surgical materials required are 10 cc. of a 10 per cent solution of n-methyl-cyclohexenyl-methylmalonylurea; an intravenous syringe; two special needle guides, 17 gage, 10 cm. long, with stylets; an 11 cm. infiltration needle, fitting exactly inside the guides; a 2 cc. syringe to fit; two pairs of gloves; procaine hydrochloride; 5 per cent phenol or absolute alcohol, and plenty of sponges and towels.

The roentgenographic equipment consists of an adequate tube which can be used under the patient's head, preferably at a slight inclination, and a suitable support for the cassette above the patient's face—a Mayo table will do.

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1. Harris, W.: Observations on the Treatment of Trigeminal Neuralgia: Alcohol Injection or Operation, Brit. M. J. **2**:87, 1932.

2. Härtel, F. F.: Zur Punktion des Ganglion Gasseri, Zentralbl. f. Chir. **60**:310, 1933.

3. Irger, I. M.: Alcohol Injections of Gasserian Ganglion for Trigeminal Neuralgia, Ann. Surg. **100**:61, 1934. Zander, P.: Erfahrungen bei Trigeminusneuralgie, insbesondere mit der Ganglionverödung nach Härtel, Arch. f. klin. Chir. **178**:242, 1933.

4. Zenker, R.: Die Behandlung der Trigeminusneuralgie durch Tiefenelektrokoagulation des Ganglion Gasseri nach Kirschner, Med. Welt **8**:14, 1934.

5. Stiasny, H.: Alkoholinjektion in das Ganglion Gasseri bei Kieferkarzinomen unter Röntgenkontrolle, Zentralbl. f. Chir. **60**:1764, 1933.

6. This anesthetic has been widely used in Germany with few reported fatalities. It was supplied by the Winthrop Chemical Company of New York.

The patient need not be fasting and is given no preliminary medication. He is strapped on the operating table, and a 10 per cent solution of the anesthetic is injected slowly into a vein until he is in deep enough sleep not to respond to a vigorous pinprick. From that point on, prompt action and teamwork are necessary. The entire face is rapidly sponged off with alcohol. The operator inserts his left forefinger into the patient's cheek on the affected side and palpates the last upper molar and the ascending ramus of the mandible. The needle guide is inserted at the angle between the ascending ramus and the malar bone and pushed mesially and upward between the buccal mucosa and the mandible until it reaches the floor of the skull. Gloves should be changed as soon as the point is past the mucosa. These are essentially the instructions given by Härtel,[2] who suggested aiming the needle toward the tubercle of the zygoma as viewed from the side and toward the pupil of the eye as viewed from in front. The tubular guide is

Fig. 1.—Roentgenogram taken during an injection into the gasserian ganglion, showing a brass needle guide inserted within the foramen.

maneuvered until it can be felt to sink through the foramen. This usually causes a characteristic slight jerk of the lower jaw. The distance from the point of puncture to the foramen is the same as that from the point of puncture to the tubercle of the zygoma, as pointed out by Gama.[7] This measurement is most conveniently made with the duplicate guide.

As soon as the needle guide is felt to be in the foramen the stylet may be removed and replaced by the long needle. From 0.25 to 0.5 cc. of 1 per cent procaine hydrochloride is injected. The inner needle is withdrawn, and a roentgenogram is taken along the axis of the needle guide (fig. 1). If the x-ray tube is in a fixed position the patient's head may be flexed backward and slightly rotated so that the needle guide is exactly vertical, and the cassette is placed at right angles to it; but it is more convenient to be able to adjust the position of both the tube

7. Gama, C.: Novos aperfeiçoamentos da technica da alcoolisaçã do ganglio de Gasser, Bol. Soc. de med. e cir. de São Paulo **13**:336, 1929.

and the cassette to the patient's head. It is advantageous to take a true lateral view also, centered on the floor of the skull, to show the depth to which the guide has penetrated (fig. 2). The films are sent to be developed at once.

By that time the effect of the anesthetic has begun to wear off, and the patient will respond to pinprick, so that it may be ascertained whether or not there is the desired anesthesia of the side of the face. If the anesthesia is complete, if no blood or spinal fluid can be aspirated and if there is no dilatation of the pupil or weakness of the external rectus muscle, the injection of phenol or alcohol may be started.

If no anesthesia results from the injection of procaine hydrochloride the probability is that the guide is not within the foramen. It is then wisest to await the return of the roentgenograms. The patient may be given more of the n-methyl-cyclohexenyl-methylmalonylurea if necessary. If the roentgenograms show that

Fig. 2.—Lateral view taken during the operation, showing the needle guide inserted through the foramen into Meckel's fossa. The needle when inserted extends 5 mm. beyond the end of the guide.

the guide is in the proper position—which is seldom difficult to judge—the depth of insertion of the long needle may be varied slightly, or the exposed portion of the guide may be pulled in one direction or another to alter the angle of insertion of the long needle. Procaine may then be injected again, and a series of trials is made until satisfactory anesthesia is produced.

If the guide is not within the foramen it should not be disturbed, but instead the duplicate guide should be inserted in the direction required, which is usually visualized without difficulty with the aid of the roentgenogram. Another roentgenogram should be taken, however, to verify the position of the second guide, and all the other precautions should be observed.

If blood or spinal fluid comes from the guide of the needle, this may be taken as an indication that the guide is in the foramen but that the long needle is in too deep or was inserted in the wrong direction. Of course, no injection should be made. The guide should be manipulated so that the point of the needle lies

more laterally if blood has been obtained and nearer the base of the skull if fluid has issued. If a spot can be found where neither is encountered, procaine hydrochloride may be injected and then the destructive agent if satisfactory anesthesia is obtained.

It is usually advantageous to allow the patient to recover sufficiently from the general anesthesia to make sure that the ganglion is completely blocked with procaine and that the pain of which he complained is relieved. This is particularly important in cases of atypical neuralgia and migraine.

Various fluids may be used as destructive agents. Alcohol (which need not be absolute) has been employed by a number of surgeons and is often satisfactory. It is, however, difficult to obtain complete anesthesia by using it, particularly to destroy the root of the second division. The tendency of alcohol to anesthetize the first division rather than the second has been pointed out by Harris.[1] Quinine and urea hydrochloride and a saturated solution of urea appear to have much the same effect as alcohol. Not more than 1.5 cc. should be used. Four per cent formaldehyde is an extremely drastic agent but hard to control. Its use has resulted in complete anesthesia but in two cases in paralysis of the abducens also. The substance which we prefer in most cases is 5 per cent phenol, which has the advantage that it affects the second division before the first and that extremely small amounts—0.5 cc. or less—are effective.

No particular after-care is ordinarily required unless the cornea has been anesthetized, in which case the customary precautions must be taken to prevent the development of keratitis. The patient is usually permitted to go home a day or two after the injection.

RESULTS

Injections have been made according to this technic in eighteen cases of trigeminal neuralgia and four cases of carcinoma of the mouth, with relief of pain in all but one. In that instance no anesthesia was produced after two attempts, and the patient was finally subjected to subtotal section of the root, which, however, left her with an extremely annoying burning sensation in the anesthetized area. In each of four other instances two attempts had to be made before the desired results were obtained. The degree of anesthesia varied with the substance injected, but the area of distribution of the third division of the nerve was always anesthetized. Alcohol or quinine and urea hydrochloride regularly produced a varying degree of hypesthesia of the first division in addition; phenol produced some hypesthesia of the area of distribution of the second division but rarely of the first. Formaldehyde produced erratic effects and was abandoned. The homolateral muscles of mastication were invariably paralyzed, but that function has begun to return in some of the patients who were operated on first.

A woman aged 80 was given an injection by this method for extremely painful postherpetic neuralgia of the first division of the trigeminal nerve of four years' standing. The pain was greatly lessened though not entirely relieved.

Injection into the ganglion was carried out in three patients with atypical migrainoid pain localized on one side of the face and centered

about the eye. One of these patients was relieved to such an extent that she returned to normal activity after having been almost entirely confined to her room for several years. A second patient has continued to have attacks of pain but only in the unanesthetized area and is to return for a second injection. The third patient continued to have pain even when the same side of the face was completely anesthetized with procaine. Accordingly, only a minute quantity of alcohol was injected, and no improvement in the condition was obtained.

DANGERS AND COMPLICATIONS

There has been one death in the series. A woman aged 60 with hypertension, nephritis and macrocytic anemia was having excruciating neuralgic pains in the area of distribution of all three divisions of the right trigeminal nerve which were relieved only by the largest doses of morphine. Section of the root was out of the question; she could not cooperate sufficiently for an injection into the peripheral portions of the nerve, and the pain was having an alarming effect on her general condition. Recognizing the danger involved, we performed an intraganglionic injection. The patient was relieved of pain but died four days later, apparently of uremia.

Another patient, a man, who also had nephritis, remained under the anesthetic for forty-eight hours. Weakness of the sixth and seventh nerves resulted in two patients who were given injections of formaldehyde (which was abandoned on that account). In one of those cases severe keratitis developed. No such complication occurred when alcohol or phenol was used.

A headache lasting for several days was often observed. Several annoying hematomas developed. The paresthesias of the anesthetic area appeared to be less annoying than those that occur after section of the root.

The danger of forcing liquid beyond the posterior root and over the pons appears to be minimal if the needle is not inserted more than 1.5 cm. beyond the foramen ovale and if the volume of fluid is kept below 1.5 cc. Experiments on the cadaver show that this is the approximate capacity of the sheath of the ganglion and its root. Very gradual injection, a drop at a time, over a period of an hour or two, as recommended by Harris,[1] appears to give complete protection against that risk.

SUMMARY

A modification of Härtel's method of injection into the gasserian ganglion is described in which the puncture is made during a brief period of anesthesia and the position of the needle is established by means of roentgenograms taken during the procedure. This has been

carried out in eighteen cases of trigeminal neuralgia, four cases of carcinoma of the mouth and one case of postherpetic neuralgia, with the obtaining of relief in all but one case. Of three patients with migraine, one was satisfactorily relieved, another was improved and a third was unaffected. The new method appears to have certain advantages over operative section of the posterior root and also over the older methods of injection. It remains for further experience to show the indications and contraindications for the employment of this method.

EXPERIMENTAL PTOSIS IN PRIMATES

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The upper eyelid is raised by the action of the levator palpebrae superioris and Müller's palpebral muscle. The former is innervated by the oculomotor nerve and the latter by fibers from the cervical portion of the sympathetic trunk. Ptosis of the upper lid follows paralysis of either nerve supply, that due to a lesion of the oculomotor nerve being greater than the slight droop which is seen in Horner's syndrome [1] due to involvement of the cervical portion of the sympathetic trunk (figure, *A*). Likewise, there is limitation of the upward excursion of the lid when the eyeball is elevated in disorders referable to the oculomotor nerve while in disturbances of the sympathetic innervation the amplitude is normal. With section of the third nerve mydriasis occurs as well as external and internal ophthalmoplegia, while a lesion of the sympathetic trunk causes miosis and enophthalmos.

This communication deals with ptosis produced experimentally in subhuman primates. Dogs and cats were observed for comparative purposes. The study was made on account of the failure to recognize a monkey which previously had been distinguished from its cagemates by ptosis due to involvement of the oculomotor nerve. Recovery from the ptosis occurred four weeks after operation far sooner than one might have anticipated regeneration of the severed nerve. Another experience indicated the importance of the sympathetic innervation when the half-closed eye of a monkey with the oculomotor nerve sectioned two weeks previously opened fully during extreme fright in a chase about the cage. The upper lid drooped again when the period of excitement passed.

OBSERVATIONS

In thirty-five animals (one chimpanzee, twenty-three monkeys, eight dogs and three cats) one oculomotor nerve was transected by a subtemporal approach.

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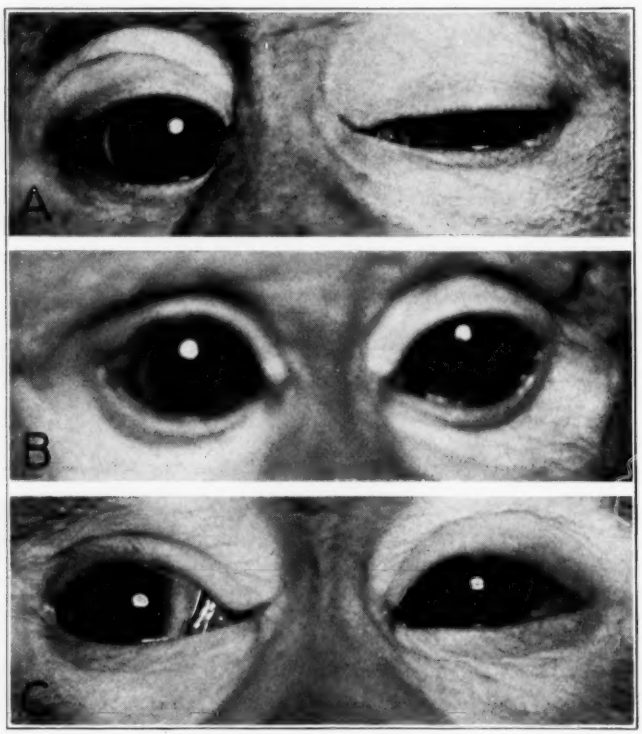
Read before the Section on Nervous and Mental Diseases at the Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1935.

1. Horner, J. F.: Ueber eine Form von Ptosis, Klin. Monatsbl. f. Augenh. **7**:193, 1869.

On the following day the corresponding eye was completely closed in the primates and almost closed in the cats and dogs. Within forty-eight hours after operation the cats were able to raise the affected eyelid almost to the full extent. The dogs showed a similar rapid recovery, but some drooping of the upper lid could be observed during the first ten days after operation. In the monkeys there was complete closure for three days and then a gradual elevation of the lid until the eye was fully open after from two to three weeks. In the chimpanzee ten days after division of the right oculomotor nerve the right eye was still completely closed. The animal died on the tenth postoperative day. Further studies on



A shows ptosis on the right side following excision of the right superior cervical sympathetic ganglion and ptosis on the left side following division of the left oculomotor nerve. *B* shows recovery from palsy of the oculomotor nerve three and one-half months after division of the right third cranial nerve. Evidence of overaction of the sympathetic innervation is still manifest by excessive retraction of the upper lid, exophthalmos and widely dilated pupil. Note recovery from the external squint. *C* shows elevation of the right upper lid during fright after bilateral extirpation of the superior cervical and stellate ganglia and division of the right oculomotor nerve.

chimpanzees have not yet been made, but the experiment demonstrates the difference in time in the persistence of ptosis following transection of the third nerve.

During the first six weeks after division of the oculomotor nerve in monkeys, section of the cervical portion of the sympathetic trunk on the same side, with

or without excision of the superior cervical and stellate ganglia, resulted in closure of the upper eyelid. The closure was not permanent, but the results of section of the sympathetic trunk manifested themselves by persistent slight ptosis, enophthalmos and a pupil smaller than it had been after division of the oculomotor nerve alone.

It was suspected that partial regeneration of the third nerve might have occurred, especially as section of the cervical portion of the sympathetic trunk with excision of the superior cervical and stellate ganglia six weeks or more after division of the homolateral oculomotor nerve did not cause closure of the eye. This suspicion was confirmed in three monkeys by exposure and transection of the united ends of the previously divided third nerve six weeks, two and three and one-half months, respectively, after primary division. In all instances secondary section was followed by complete ptosis.

Further evidence of regeneration of the divided oculomotor nerve was obtained by allowing recovery from the palsy of the third nerve to continue in two monkeys without interference. Three months after such an operation the external squint had disappeared and the eyeball could be moved voluntarily in all directions, but with a definite lag upward and downward as compared with the control eye. Horizontal movements occurred synchronously in both eyes. Reactions to light and in accommodation could be elicited but were very poor even after eight months. The ptosis had disappeared completely, but there was a lag in the elevation of the upper eyelid. Some overactivity of the sympathetic innervation was, however, still manifest, as shown by the extreme dilatation of the pupil, excessive retraction of the upper lid and exophthalmos (figure, *B*).

Before recovery from the ptosis following division of the oculomotor nerve the eye could be opened widely whenever the animal was frightened, as was evidenced when the monkeys were caught for close examination. Greater dilatation of the pupil invariably occurred on the side of the operation than in the control eye under such circumstances. The instantaneous opening of the normal eye contrasted markedly with the more gradual elevation of the upper lid of the ptotic eye. Thirty seconds elapsed before the eye was completely open, and after about two or three minutes the upper lid spontaneously and slowly returned to its ptotic position. Excision of the homolateral superior cervical and stellate ganglia did not prevent this response to fright; indeed, the elevation of the upper lid and the dilatation of the pupil were actually greater than before extirpation of the sympathetic ganglia.

The possibility of sympathetic fibers reaching the smooth muscle of the upper lid from the sympathetic trunk of the opposite side was excluded by bilateral removal of the superior cervical and stellate ganglia in a monkey with a recently transected third nerve. The eye still opened widely under conditions of extreme fright, and there was again manifest the extreme retraction of the upper lid with greater dilatation of the same pupil.

The phenomena observed during states of extreme excitement indicated a profuse discharge from the adrenal glands as the possible causative factor. Epinephrine chloride in doses of 2 cc. of a 1: 1,000 solution was therefore injected intramuscularly into the animals in which the third nerve had been transected and the cervical sympathetic chain on both sides completely removed. The ptotic lid which had elevated under the animal's fright on being caught and given an injection closed again slowly when the monkey was returned to the cage. Within five minutes the animal became prostrate, with respiratory and cardiac rates markedly accelerated, and the ptotic eye opened widely with maximum dilatation of the pupil. This state persisted for a quarter of an hour and then gradually subsided.

During the first two days after transection of the oculomotor nerve neither fright nor the injection of epinephrine had any effect on the complete ptosis. The day following removal of the sympathetic ganglia there was invariably a maximal elevation of the ptotic lid after fright or injection of epinephrine.

With the animal under sodium amytal anesthesia the control eye was closed and the pupil small. In contrast, the eye in which the third nerve had been divided at a previous operation was open and the pupil widely dilated. Excision of the cervical sympathetic ganglia did not alter this phenomenon.

The following protocols will indicate the chronology of events in two experiments on monkeys:

PROTOCOLS

Observation 1.—An immature male rhesus monkey (Macaca mulatta); weight, 2.65 Kg.

Oct. 1, 1934: Intracranial transection of the right oculomotor nerve was carried out.

October 2: Complete closure of the right eye with internal and external ophthalmoplegia was noted. It was impossible to raise the right upper eyelid, either after fright or after the intramuscular injection of 2 cc. of a 0.1 per cent solution of epinephrine chloride.

October 4: Complete ptosis of the right upper eyelid was noted, but when the monkey was caught for close examination the right eye opened slightly.

October 5: The right eye was open one-quarter while the animal was undisturbed; during fright the lid was elevated to the middle of the pupil, but it returned to the almost closed position in two or three minutes.

October 6: The right eye was half open. Fright resulted in a greater widening of the palpebral fissure. Intramuscular injection of 2 cc. of a 0.1 per cent solution of epinephrine chloride produced the same but more lasting effect.

October 15: The right eye was fully open while the animal remained undisturbed in the cage. External and internal ophthalmoplegia were still present.

October 22: The condition was unchanged. Voluntary movement of the eyelids was much better performed on the left than on the right side. On sudden upward gaze the left upper eyelid moved rapidly, but the right lid lagged behind and its movement was much slower, although there was ultimately a wider palpebral fissure on the right than on the left side.

November 15: There were extreme retraction of the right upper eyelid and slight exophthalmos, and the pupil was wider in the right than in the left eye. External and internal ophthalmoplegia were still present. The right eye could be moved laterally and brought back to the midline, but there was complete inability to turn the eye medially.

December 2: The condition of the right eye was essentially the same.

December 22: Horizontal movements of the right eye, both laterally and medially, were evident, but the eyes did not move synchronously. There was immobility of the right eye in upward and downward gaze.

Jan. 18, 1935: The external squint of the right eye had completely disappeared, and the right eyeball moved voluntarily in all directions but with a definite lag in upward and downward gaze. Horizontal movements were synchronous in the two eyes. Reactions to light and in accommodation were not present in the right eye. Evidence of overactivity of the sympathetic innervation was shown by extreme dilatation of the pupil, excessive retraction of the upper lid and exophthalmos (figure, *B*).

January 19: Extirpation of the right superior cervical sympathetic ganglion was carried out.

January 20: There was slight ptosis of the right upper lid, and the right pupil was smaller.

January 24: Intracranial transection of the reunited right oculomotor nerve was carried out.

January 25: There was complete closure of the right eye, with internal and external ophthalmoplegia.

OBSERVATION 2.—An immature female rhesus monkey (Macaca mulatta); weight, 2.8 Kg.

Jan. 21, 1935: Intracranial division of the right oculomotor nerve was carried out.

January 22: There was complete closure of the right eye, with internal and external ophthalmoplegia. There was no effect on the right upper lid after fright or after the intramuscular injection of 2 cc. of a 0.1 per cent solution of epinephrine chloride.

January 24: The right eye was slightly open; 2 cc. of a 0.1 per cent solution of epinephrine chloride was injected intramuscularly. The right upper eyelid was elevated during the injection but drooped again when the animal was returned to the cage. Within five minutes the respiratory and cardiac rates accelerated markedly, and the right eye opened widely, with maximum dilatation of the pupil. The condition persisted for fifteen minutes and then gradually subsided, and the right upper lid returned to the ptotic position.

February 7: The right eye was almost fully open when the monkey was in the quiescent state. External squint and mydriasis were obvious. There was a similar response to fright and to the intramuscular injection of epinephrine.

February 8: Section of the cervical portion of the right sympathetic trunk was carried out.

February 9: There was marked but incomplete ptosis of the right upper lid, and the right pupil was smaller. The response to fright and to the intramuscular injection of epinephrine was unaltered.

February 11: Extirpation of the right superior cervical sympathetic ganglion was carried out.

February 12: Ptosis of the right lid was not increased.

February 18: The condition was unchanged. Elevation of the right lid and dilatation of the right pupil during fright or after the injection of epinephrine was now greater in degree than before ganglionectomy. External and internal ophthalmoplegia were present.

February 20: Intracranial division of the scar tissue was performed, and the cut ends of the right third nerve were united.

February 21: The condition was unchanged.

February 25: Extirpation of the right stellate ganglion was carried out.

February 26: The condition of the right upper lid was unchanged. It was still excessively retracted during fright or after the injection of epinephrine.

March 6: Extirpation of the left stellate ganglion was carried out.

March 7: The condition of the right upper lid was unchanged.

March 14: Extirpation of the left superior cervical sympathetic ganglion was carried out.

March 15: The condition of the right upper lid was unchanged. There were excessive retraction of the right upper lid, extreme dilatation of the right pupil and slight exophthalmos during fright or after the injection of epinephrine. External and internal ophthalmoplegia were present.

COMMENT

Sherrington's [2] experimental work on ptosis after intracranial section of the third nerve in monkeys indicated that "the eyelid dropped permanently to the middle of the pupil." Adler,[3] in discussing the clinical physiology of the eye, stated:

> It might be imagined that when the levator was paralyzed the upper lid would be kept from drooping by the smooth muscle innervated by the sympathetic. Unfortunately this does not occur due to the fact that the smooth muscle fibers take their origin from the under surface of the levator. When this is paralyzed the smooth muscle fibers have no firm point of origin from which to work, and their contraction becomes ineffective. The ptosis is, therefore, complete.

The results presented in this communication show that such a view is not applicable to animals as high in the phylogenetic scale as subhuman primates. The rapid recovery from ptosis due to lesion of the oculomotor nerve and the immediate reappearance of the ptotic state on removal of the cervical sympathetic ganglia indicate that unaided the sympathetic innervation can elevate the upper lid. The observations suggest an important synergic action of the cervical portion of the sympathetic trunk and the third cranial nerve. It has been known since the time of Pourfour du Petit [4] that section of the cervical portion of the sympathetic trunk results in slight ptosis but the power of the palpebral involuntary musculature alone to open the eye has hitherto not been recognized.

Groyer [5] offered the following interpretation of the morphology of the palpebral involuntary musculature: In aquatic mammals each of the four rectus muscles divides into two lamellae, the inner inserted onto the globe and the outer entering the eyelid. Both lamellae are composed of striated muscle fibers. In higher mammals and in man the outer palpebral lamellae are replaced by smooth muscle fibers except in the case of the superior rectus muscle. Here the outer or palpebral lamella remains partly striated, forming the levator palpebrae superioris, and only the deeper part becomes converted into smooth muscle fibers and is called the superior muscle.

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2. Sherrington, C. S.: Experimental Note on Two Movements of the Eye, J. Physiol. **17**:27, 1894.

3. Adler, F. H.: Clinical Physiology of the Eye, New York, The Macmillan Company, 1933, p. 5.

4. du Petit, François Pourfour: Mémoire dans lequel il est démonstré que les nerfs intercostaux fournissent des rameaux qui portent des esprits dans les yeux, Hist. Acad. roy. d. sc. Paris **1**:1, 1727.

5. Groyer, F.: Zur vergleichenden Anatomie des Musculus orbitalis und der Musculi palpebrales, Sitzungsb. d. k. Akad. d. Wissensch. Math.-naturw. Cl. **112**: 51, 1903; Zur Anatomie des Musculus palpebrae superioris des Menschen, Ztschr. f. Augenh. **14**:365, 1905.

The superior palpebral involuntary muscle, according to Whitnall,[6] lies in close contact with the under surface of the levator muscle. The fibers arise from between the striated fibers of the levator muscle and are attached to the upper margin of the tarsal plate. It is said to be innervated entirely by fibers from the cervical portion of the sympathetic trunk by way of the cavernous plexus, although the presence of groups of nerve cells intermingled with the muscle fibers, described by Groyer [5] in 1905, suggests a possible additional innervation from the parasympathetic system through the third nerve.

The more rapid recovery from ptosis due to palsy of the third nerve in cats and dogs as compared with monkeys, and in monkeys as compared with the chimpanzee, suggests a progressively increasing importance of the sympathetic innervation as one descends the phylogenetic scale.

There is a differential rate of recovery of the functions of the third nerve during regeneration. Even after positive steps are taken to interfere with union, as by excision of 2 or 3 mm. of this nerve, evidence of regeneration is manifest at the end of six weeks. The reestablishment of function occurs first in the ability to raise the upper eyelid and at a slightly later date in the movements of the extra-ocular muscles. The parasympathetic innervation of the pupil and of the ciliary body shows few if any signs of regeneration, as evidenced by the extreme and persistent dilatation of the pupil and by the scarcely perceptible reaction to light and in accommodation eight months after section of the third nerve. The explanation of this difference appears clear when one considers the more intricate route for the regenerating axis-cylinders of the parasympathetic division of the third nerve. These fibers must necessarily find their way along the remains of the sheaths of the fine short ciliary nerves, and, in addition, accurate synaptic connections must be established with the postganglionic cells situated in the ciliary ganglion.

Even in the complete absence of innervation from the third nerve and the cervical portion of the sympathetic trunk, elevation of the upper lid can take place, but only under conditions of extreme excitement or following the injection of epinephrine. In such animals all postganglionic neurons of the cervical portion of the sympathetic trunk have been extirpated from both sides. As there appears no other obvious pathway for sympathetic fibers to the smooth muscle of the upper eyelid, these results indicate that epinephrine acts directly on the muscle fiber. It might be supposed that nerve fibers reach the smooth musculature of the eye by way of the sixth or seventh cranial nerve and are

6. Whitnall, S. E.: The Anatomy of the Human Orbit, ed. 2, New York, Oxford University Press, 1932.

still present after bilateral extirpation of the cervical sympathetic ganglia. If such is the case, the concept of a pure thoracolumbar outflow of the sympathetic nervous system cannot hold, for such presumed fibers would be clearly adrenotropic, as evidenced by the response to fright and to injections of epinephrine.

The elevation of the ptotic eyelid of a subject with palsy of the oculomotor nerve after fright or the injection of epinephrine is complete, but following removal of the cervical sympathetic ganglia it is still more marked and exceeds the elevation of the opposite eyelid. There are, in addition, exophthalmos and wider dilatation of the pupil than in the control eye. Such an increased response of the smooth musculature of the eye following removal of all postganglionic sympathetic neurons confirms the earlier observations on the "paradoxical" pupillary dilatation. In 1855 Budge [7] noted that the pupil was larger after section of the postganglionic fibers above the superior cervical ganglion than when the cervical portion of the sympathetic trunk was cut. Langendorff,[8] among others, in confirming the findings of Budge [7] named the phenomenon the *paradoxe Pupillenerweiterung*. Lewandowsky [9] in 1899 demonstrated for the first time that intravenous injection of an adrenal extract caused widening of the pupil, retraction of the nictitating membrane, elevation of the upper eyelid and exophthalmos. Division of the cervical portion of the sympathetic trunk and extirpation of the superior cervical ganglion brought the reaction out better. Lewandowsky considered that the adrenal extract acted directly on the smooth muscle. Langley [10] confirmed the findings of Lewandowsky [9] and agreed with his interpretation. He added that division of the third nerve intracranially or ligature of the short ciliary nerves peripheral to the ciliary ganglion made no essential differences to the action of adrenal extract injected intravenously and that there was similar overactivity of the erector pili muscles after degeneration of all postganglionic sympathetic fibers. Anderson [11] in 1904 reported that excitement, dyspnea and anesthesia were the conditions which evoked the paradoxical response.

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7. Budge, J.: Ueber die Bewegung der Iris, Braunschweig, Fr. Vieweg u. Sohn, 1855; cited by Langendorff.[8]

8. Langendorff, O.: Ueber die Beziehungen des oberen sympathischen Halsganglions zum Auge, Klin. Monatsbl. f. Augenh. **38**:129, 1900.

9. Lewandowsky, M.: Ueber die Wirkung des Nebennierenextractes auf die glatten Muskeln, im besonderen des Auges, Arch. f. Physiol. 1899, p. 360; Ueber das Verhalten der glatten Augensmuskeln nach Sympathicusdurchschneidung, ibid. 1903, p. 367.

10. Langley, J. N.: Observations on the Physiological Action of Extracts of the Suprarenal Bodies, J. Physiol. **27**:237, 1901.

11. Anderson, H. K.: Reflex Pupil-Dilatation by Way of the Cervical Sympathetic Nerve, J. Physiol. **30**:15, 1904; Special Reference to the Occurrence of Paradoxical Contraction, ibid. **30**:290, 1904.

He also concluded that there was no evidence of efferent fibers reaching the iris other than by way of the cervical portion of the sympathetic trunk and the third cranial nerve. These phenomena have been confirmed, and the subject has been adequately reviewed by Meltzer and Auer [12] and Elliott.[13]

It is clear that epinephrine acts directly on smooth muscle or, as Elliott [13] suggested, at a myoneural junction depending for continuance of life on the muscle and not on the nerve cell. That smooth muscle when deprived of postganglionic sympathetic fibers shows a greater irritability to epinephrine than it previously possessed is a phenomenon still unexplained. The important clinical application of this sensitization of smooth muscle by extirpation of the sympathetic ganglia has been emphasized recently in connection with peripheral vascular disorders by Smithwick, Freeman and White.[14]

Observation of the upper eyelid offers a readily accessible method for investigating the influence of the sympathetic nerve supply on smooth muscle and of the action of epinephrine on the same muscle after removal of its sympathetic innervation. This mechanism has been studied in animals as high as subhuman primates and has revealed an individual power of the sympathetic innervation more effective than has been generally supposed. The earlier observation of greater sensitivity of denervated smooth muscle to epinephrine has been confirmed. The possible application to human physiology awaits clinical studies along these lines in cases of palsy of the oculomotor nerve.

SUMMARY

Intracranial division of the oculomotor nerve in animals is followed by ptosis of the upper eyelid, with more rapid recovery as one descends the phylogenetic scale.

Recovery from the ptosis of palsy of the oculomotor nerve depends on the cervical portion of the sympathetic nervous system during the first six weeks. After this period regeneration of the fibers of the third nerve to the levator palpebrae superioris muscle occurs.

Before recovery from such ptosis is complete the upper eyelid can be raised during extreme excitement or after the injection of epinephrine. After bilateral extirpation of the superior cervical and stellate ganglia this phenomenon is still present and is manifest to a greater degree.

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12. Meltzer, S. J., and Auer, C. M.: Studies on the "Paradoxical" Pupil-Dilatation Caused by Adrenalin, Am. J. Physiol. **11**:28, 37 and 40, 1904.

13. Elliott, T. R.: The Action of Adrenalin, J. Physiol. **32**:401, 1905.

14. Smithwick, R. H.; Freeman, N. E., and White, J. C.: Effect of Epinephrine on the Sympathectomized Human Extremity, Arch. Surg. **29**:759 (Nov.) 1934. Freeman, N. E.; Smithwick, R. H., and White, J. C.: Adrenal Secretion in Man, Am. J. Physiol. **107**:529, 1934.

ABSTRACT OF DISCUSSION

DR. R. GLEN SPURLING, Louisville, Ky.: I have observed six cases of complete paralysis of the third nerve. In four the patient had aneurysm of the basilar arteries; in one there was a suprasellar meningioma, and in another, a pituitary adenoma which had escaped the boundaries of the sella turcica. These cases were observed over a period of months or years. Recovery of function was invariably slow. In some cases a year or more elapsed before the signs and symptoms of paralysis of the third nerve disappeared, and in one patient, with pituitary adenoma, the partial paralysis has persisted over a period of six years. It is my impression that ptosis associated with such lesions improves more rapidly than does paralysis of the extrinsic and intrinsic muscles of the eye. However, several weeks or months elapsed before any noticeable improvement in ptosis occurred. Heretofore I have attempted to explain the improvement in ptosis on the assumption that the fibers to the levator palpebrae superioris muscle regenerate more quickly than do the rest of the fibers. However, in view of this work it would seem more likely that the early improvement in ptosis is due to the action of Müller's palpebral muscle innervated through the cervical portion of the sympathetic trunk.

THE CONVULSION THRESHOLD OF VARIOUS PARTS OF THE CAT'S BRAIN

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AND
ERNA L. GIBBS
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In this investigation we have attempted to determine the relative ease or difficulty with which convulsions can be produced by electrical stimulation of various parts of the cat's brain. The problem has significance because it bears directly on the question of whether or not a special part of the brain is concerned with the production of convulsions, a question of major importance to those interested in the etiology of epileptic seizures.

METHOD

With a cat under ether anesthesia a 24 gage needle electrode of the type used by Adrian and Bronk[1] was inserted into the brain through a perforated metal plug screwed into a small bur hole in the skull. This type of electrode is made by running an insulated wire through a hollow needle, such as is used for venipuncture or subcutaneous injection, and by sealing the wire in place. In our experiments the wire in the needle was used as the stigmatic electrode; no connections were made to the needle itself. A large indifferent electrode was strapped over a shaved area on the cat's back. Two hours after the discontinuation of the ether, the needle electrode was connected to one terminal of the secondary coil of a Harvard inductorium having an iron core in the primary coil. The other terminal of the secondary coil was connected to the indifferent electrode. Current from a 1.5 volt dry cell was supplied to the primary coil through the interrupter. The strength of the stimulus was varied by changing the position of the secondary coil. Each stimulation lasted five seconds. Note was taken of the first movement elicited by stimulation and of the threshold strength of the stimulus necessary to elicit it. The strength of the stimulus was expressed in terms of centimeters of distance of the end of the primary coil nearest the interrupter from the end of the secondary coil nearest the interrupter. After the threshold for the first movement had been determined, the strength of stimulation was increased in steps of 5 mm. Each stimulation lasted, as has been stated, five seconds. An interval of three minutes was allowed between stimulations. The strength of stimulus was

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1. Adrian, E. D., and Bronk, D. W.: The Discharge of Impulses in Motor Nerve Fibers, J. Physiol. **67**:119, 1929.

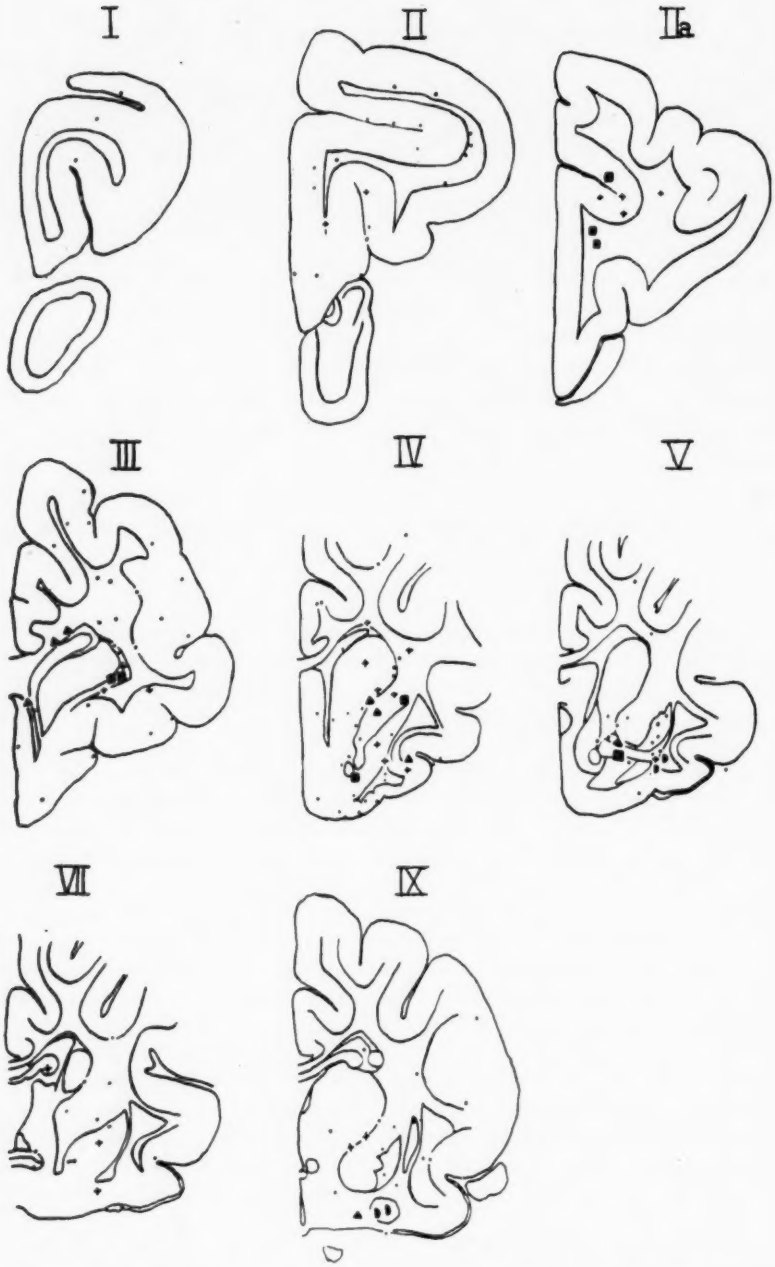
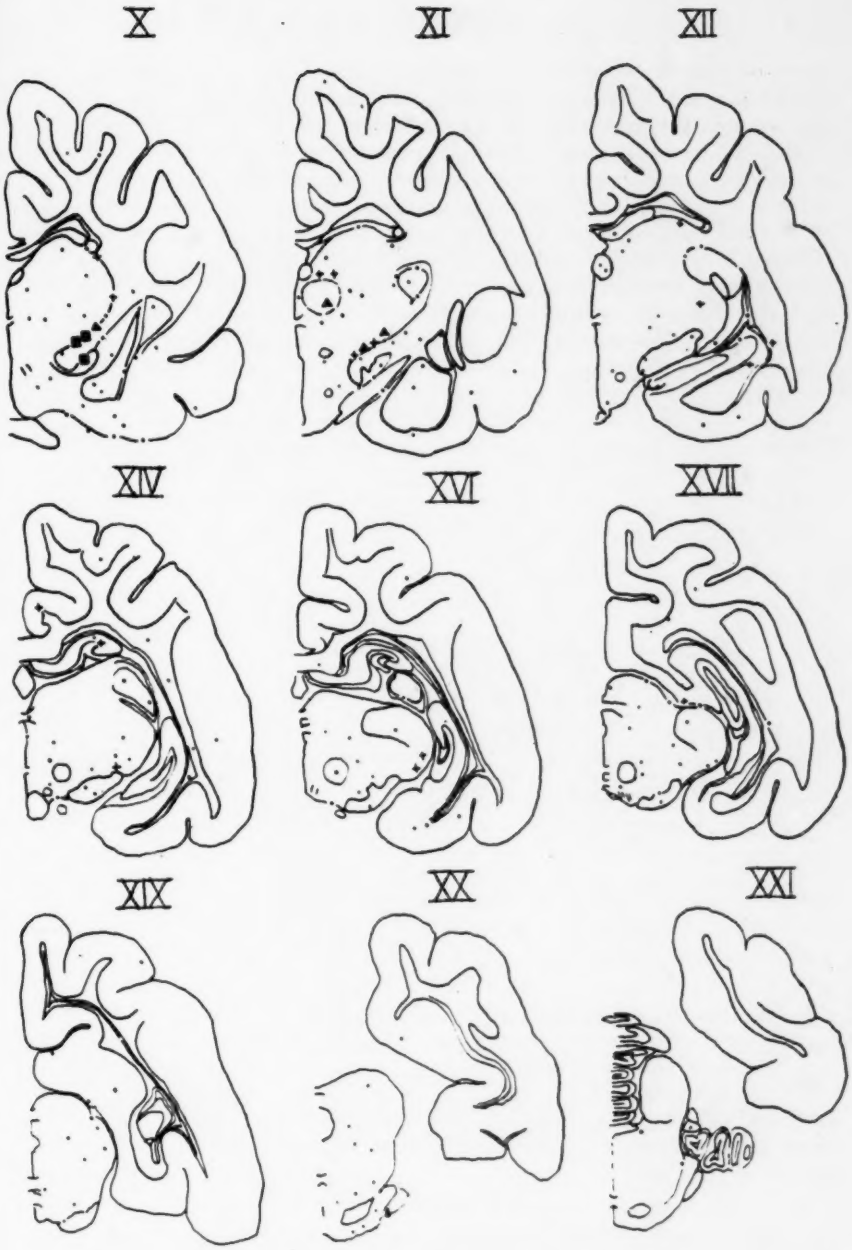


Fig. 1.—Line drawings made from the plates in Potter and Winkler's "Atlas of the Cat's Brain," with the exception of section *IIa*, which was added to fill a gap in the Potter and Winkler series. Certain of the plates (Potter and Winkler) on which sections are shown close together were omitted; the numbers of the figures correspond with those of the plates. The points stimulated in 348 experiments, each on a different animal, are indicated by the dots, crosses, solid semicircles, triangles and squares. The significance of these in terms of coil distance is as follows: occurrence of a convulsion with the coil at from 11.5 to 10 cm., solid square; at from 9.9 to 9.5 cm., solid triangle; at from 9.4 to 9 cm., cross;



at 8.9 cm., dot, which also indicates that no convulsion was elicited. A facial convulsion occurred when the coil was at from 11.5 to 10 cm., solid semicircle. Obviously, the areas indicated by solid squares and triangles are those of most interest in relation to the genesis of convulsions. They tend to fall into line in such a way as to suggest a short fiber system linking the frontal cortex with the thalamus and possibly with the basal ganglia. If the crosses, representing areas with somewhat lower thresholds, are considered, a second system stands out, which appears to be associated with the amygdaloid nucleus, fornix, gyrus fornicatus and alveus.

increased until it precipitated a convulsion. Our criteria for a convulsion were: a series of violent movements continuing after stimulation, not purposeful in nature and usually accompanied by disorders of ocular movements, such as the turning of the eyes far to the side or fixity of gaze, and by overflow of saliva from the mouth. If no convulsion occurred before the secondary coil was 7 cm. from the primary, stimulation was discontinued. At the termination of the experiment, all animals were immediately killed with chloroform; the brain was removed and hardened in solution of formaldehyde. The location of the tip of the needle was determined by free-hand sections. When the threshold for a convulsion was very low or when the tip of the needle was found to lie near a region which had previously shown a low threshold, the exact position of the needle was determined from stained serial sections.

Three hundred and forty-eight successful experiments were conducted. In each case only one needle was inserted into the brain and the needle was not moved, so that only one point in the brain of each animal was stimulated.

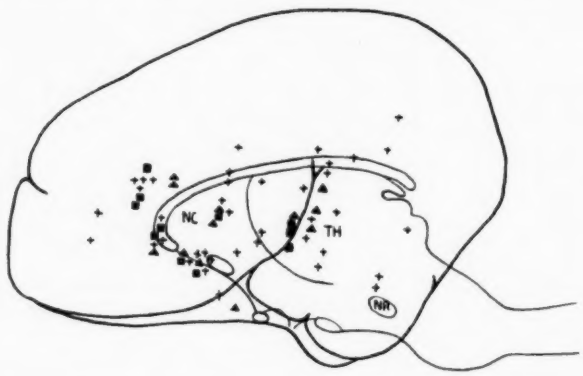


Fig. 2.—Lateral projection of the areas in the cat's brain which have a low convulsion threshold. The significance of the squares, triangles and crosses in terms of coil distance is given in figure 1. The squares are the lowest threshold areas, the triangles next, and the crosses next.

These experiments were undertaken with some misgivings because it was feared that the stimulation would produce pain before it produced a convulsion. We were therefore relieved to find that from only a very small part of the brain did weak stimulation elicit a painful reaction, and in a number of experiments we found that stimulation was apparently pleasurable, for it elicited purring and gentle wagging of the tail. The location of this "purring center" will be described elsewhere.[2]

RESULTS

The results of this investigation are best presented by diagrams. These are shown in figure 1. The areas with low thresholds are represented in lateral projection in figure 2. It may be seen that there are great differences in the convulsion thresholds of various parts of

2. Gibbs, E. I., and Gibbs, F. A.: A Purring Center in the Cat's Brain, Science, to be published.

the brain and that the areas with the lowest thresholds lie in clearly defined parts of the frontal cortex, basal ganglia, internal capsule and thalamus. Many areas on the cortex have very high thresholds, as do many areas in the white matter. The exposed surface of the sigmoid gyrus is not a low threshold area. No points with low thresholds could be found in the midbrain or cerebral peduncles. Just as high thesholds were found in areas which are believed to be essentially motor as in areas that are essentially sensory. The areas with the lowest thresholds seem to suggest a system of fibers running through the internal capsule connecting the thalamus, the frontal cortex and possibly the basal ganglia. A second system is suggested by the points with rather low thresholds along the fornix, close to the amygdaloid nucleus, in the gyrus fornicatus and near the alveus of the temporal lobe.

On several occasions convulsions confined to the face were obtained. The points from which such facial convulsions were elicited by weak stimulation are shown in the figures. They lie in or very near the anterior part of the amygdaloid nucleus.

COMMENT

There is no apparent correlation between the general type of structure stimulated and the convulsion threshold; that is, no statement can be made about the threshold of white matter as compared with that of gray matter. Nor is there any correlation between the convulsion threshold and the motor or sensory function of the tissue stimulated. Regions with a low threshold for the first motor response did not necessarily have a low threshold for convulsions. From numerous points, notably in the sigmoid gyrus, internal capsule and cerebral peduncles and parts of the midbrain, it was possible to elicit a movement with the secondary coil at 13, but no convulsion occurred until the coil was pushed down to 7, whereas from several points no movement was obtained during stimulation with the coil at 10, but a convulsion developed, nevertheless, after stimulation. Worthy of special notice is the fact that no low threshold points could be found in the midbrain or in the cerebral peduncle, which seems to indicate that the structure which produces convulsions most readily is not a long fiber system, either ascending or descending. That it is not specifically the pyramidal tract, despite the low threshold points in the posterior part of the sigmoid gyrus, is indicated by the fact that numerous high threshold points are situated close to the pyramidal tract in the internal capsule and cerebral peduncle and by the fact that numerous low threshold areas are situated in areas far removed from the pyramidal tract, notably in the pyriform cortex and the medial nucleus of the thalamus. It should also be noted that some points with rather low thresholds were found along the course

of the fornix, in the gyrus fornicatus and in the temporal lobe. In conjunction with this, the low threshold points close to the amygdaloid nucleus (fig. 1; IX) are of interest. The fornix and the taenia semicircularis, which runs close to it, connect the amygdaloid nucleus and structures near it with the temporal lobe, and there is evidence that fiber connections to the gyrus fornicatus run through the fornix.[3]

The arrangement of these low threshold areas suggests certain important negative conclusions: 1. Convulsions are not readily produced by stimulating gray matter as such, for various areas from which it was extremely difficult to obtain convulsions lie in gray matter. 2. Convulsions are not readily produced by stimulating white matter as such, for numerous high threshold areas lie in white matter. 3. Convulsions are not readily produced by stimulating cerebral blood vessels, for the low threshold areas do not lie along the course of any special blood vessel nor are they in regions which differ from other areas of the brain in vascularity. It would appear that convulsions can be produced with weak electrical stimuli only if the stimulus is applied to certain neurons in the brain. These neurons are grouped together to form a system which is at least as clearly defined as that from which electrical stimulation elicits dilatation of the pupil.[4] If the system involved is a fiber tract, it would appear to be afferent to the cortex, for the low threshold area on the medial border of the internal capsule, shown in section X of figure 1, contains chiefly afferent fibers, and parts of the thalamus which contain low threshold areas have chiefly afferent connections to the cortex. Degeneration experiments are now in progress by which it is hoped to identify the fiber tracts concerned and determine the location of their cell bodies. The present study, however, suffices to show that the essential structure implicated is a system of short fibers connecting the frontal cortex, the para-olfactory area, parts of the basal ganglia and the thalamus.

The study by one of us (F. A. G.) of a series of 300 cases of tumor of the brain with autopsy at the Johns Hopkins Hospital brought out the fact that tumors producing generalized convulsions tend to involve certain parts of the brain, a fact that was further substantiated by adding to the data obtained from this series data obtained from the analysis of 1,340 cases of tumor of the brain from the Peter Bent

3. Kappers, C. U. A.: Die vergleichende Anatomie des Nervensystems der Wirbeltiere und des Menschen, Haarlem, Netherlands, de Erven F. Bohn, 1921, vol. 2.

4. Ingram, W. R.; Ranson, S. W., and Hannett, F. I.: Pupillary Dilatation Produced by Direct Stimulation of the Tegmentum of the Brain Stem, Am. J. Physiol. **98**:687, 1931. Ranson, S. W., and Magoun, H. W.: Respiratory and Pupillary Reactions Induced by Electrical Stimulation of the Hypothalamus, Arch. Neurol. & Psychiat. **29**:1179 (June) 1933.

Brigham Hospital.[5] The results obtained from the series studied at Johns Hopkins at first suggested that tumors produce convulsions by involving a "convulsion center." Such an interpretation, however, seemed so bizarre that it was disregarded.

Since the evidence presented here tends to show that there is what might be called a "convulsion center" in the cat's brain, it seems unwise to disregard such an interpretation of data pertaining to man. The region implicated by tumors of the brain is not altogether dissimilar to that implicated by electrical stimulation of the cat's brain, as can be

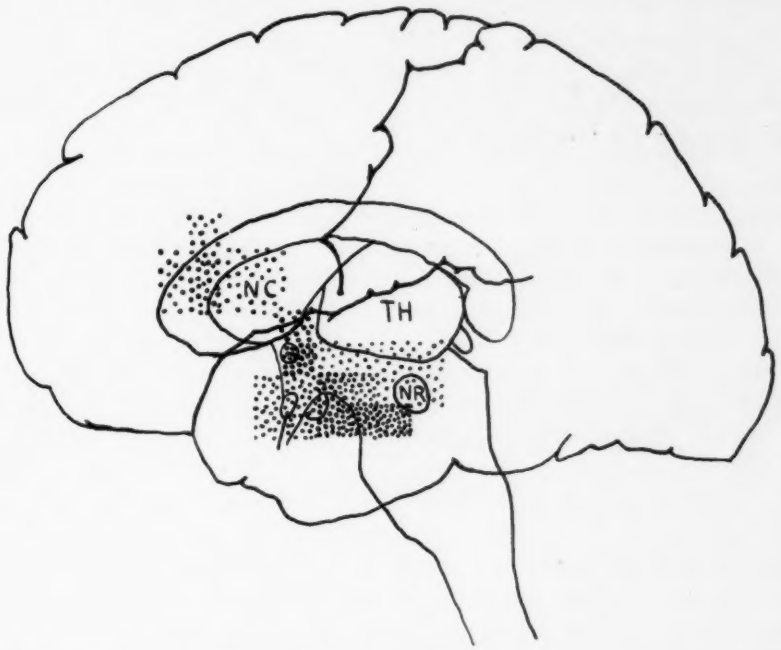


Fig. 3.—Lateral projection of the areas most frequently involved by tumors producing generalized convulsions—based on the analysis of 300 cases of tumor of the brain with autopsy from the Johns Hopkins Hospital. In 27 of the 300 cases, generalized convulsions occurred. The closely stippled areas were involved in 6 cases, the less closely stippled areas in 5 cases and the most sparsely stippled areas in 4 cases. In 23 of the 27 cases (85 per cent) there was involvement of some part of the stippled areas.

seen from the figure showing the lateral projection of the areas most frequently involved by tumors producing generalized convulsions (fig. 3). Such a figure is a construction of doubtful validity, but, whatever its demerits, if the regions in which tumors produce con-

5. Gibbs, F. A.: Frequency with Which Tumors in Various Parts of the Brain Produce Certain Symptoms, Arch. Neurol. & Psychiat. **28**:969 (Nov.) 1932.

vulsions in man were quite different from those in which electrical stimulation produces convulsions in cats, such a figure might serve to emphasize this difference. That it does not is at least suggestive.

CONCLUSIONS

1. There is a marked difference in the convulsion thresholds of various areas in the cat's brain.

2. The arrangement of the areas with the lowest thresholds suggests that the essential structure implicated is a system of short fibers connecting the thalamus, the frontal cortex and the basal ganglia.

3. If somewhat higher thresholds are taken into account, a second system is suggested which accompanies the fornix and connects the amygdaloid nucleus and surrounding area with the gyrus fornicatus and with parts of the temporal lobe.

EXPERIMENTAL STUDIES IN ALCOHOLISM

II. THE ALCOHOL CONTENT OF THE BLOOD AND CEREBROSPINAL FLUID FOLLOWING INTRAVENOUS ADMINISTRATION OF ALCOHOL IN CHRONIC ALCOHOLISM AND THE PSYCHOSES

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AND
ELMER STOTZ, B.S.
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In the first part of this investigation,[1] based on a study of fifty-two cases, we were able to demonstrate that following the oral ingestion of standard doses of alcohol certain differences exist in the curves for the alcohol content of the blood and spinal fluid, depending on the drinking habits of the subjects. It was found that in the heavy drinkers as a group the alcohol content of the blood after ingestion increases more rapidly, reaches a higher peak and decreases more quickly than in the abstainers; the values for the group of moderate drinkers occupy an intermediate position in all three respects. As far as the curves for the alcohol content of the spinal fluid are concerned, those for the heavy drinkers rise more rapidly, reach a slightly higher peak and decline more quickly than those for the abstainers; for the moderate drinkers, however, the curves for the alcohol content of the spinal fluid, instead of occupying an intermediate position as in the case of those for the blood, rise and fall more slowly than the curves for either the abstainers or the heavy drinkers. It was pointed out that these differences in the curves for the spinal fluid are of small magnitude and therefore are of questionable significance but that if confirmed they are of considerable interest in suggesting changed relationships in permeability between the blood and spinal fluid systems in cases of alcoholism. That changes in the permeability of the hemato-encephalic barrier to substances other than alcohol occur in cases of alcoholism is suggested by the work of Rothschild and Burke,[2] who

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From the Boston Psychopathic Hospital.

This paper was read in part at a Physiological Conference at the Harvard Medical School, Nov. 20, 1934.

1. Fleming, R., and Stotz, E.: Experimental Studies in Alcoholism: I. Alcohol Content of the Blood and Cerebrospinal Fluid Following Oral Administration in Chronic Alcoholism and the Psychoses, Arch. Neurol. & Psychiat. **33**: 492 (March) 1935.

2. Rothschild, D., and Burke, E. R.: Blood-Cerebrospinal Fluid Barrier in Alcoholic Disorders and in Schizophrenia Complicated by Alcoholism, Arch. Neurol. & Psychiat. **30**:141 (July) 1933.

reviewed briefly the conflicting literature on Walters' bromide test in this connection.

It occurred to us that by introducing the alcohol directly into the blood the effects of different rates of absorption from the gastrointestinal tract could be eliminated and that thus the passage of alcohol from the blood into the spinal fluid could be studied more directly. Alcohol had been administered intravenously to man without regard to the alcohol concentrations of the spinal fluid by Gabbe [3] in 1917 and by Mehrtens and Newman in 1933 [4] with a different object in view. Gabbe injected 0.3 Gm. of absolute alcohol (in a 10 per cent solution) per kilogram of body weight into ten subjects (four heavy drinkers, four moderate drinkers and two abstainers); his experiments were poorly controlled, and the results were inconclusive, so that in order to clear up the points at issue it seemed desirable to repeat this work with a larger series of subjects and to observe the alcohol concentration of the spinal fluid along with that of the blood. It was with this object in view that the work reported in this paper was undertaken.

PROCEDURE

The experimental conditions were identical with those of our previous experiments except that the alcohol was given by vein instead of by mouth. The dose (0.6 cc. by volume of absolute alcohol per kilogram of body weight) was diluted under aseptic conditions with sterile physiologic solution of sodium chloride to a strength of 20 per cent and administered into the median cephalic or the median basilic vein of the subject's right arm in the customary manner.

The time required for the dose of alcohol to run (by gravity) into the vein varied slightly but averaged six and eight-tenths minutes for all the injections. In spite of the fact that procaine hydrochloride was used intracutaneously to provide a small area of anesthesia for venipuncture, the injection was almost always accompanied by considerable pain: As the alcoholic solution runs into the vein a dull ache radiates up the arm into the shoulder, gradually increasing in severity until it is intense. Acting on the suggestion of Dr. Stanley Cobb, we investigated in nine patients the influence of the administration of alcohol (oral and intravenous) on the cerebrospinal fluid pressure. The rise of cerebrospinal fluid pressure frequently associated with intravenous administration of alcohol seems to be dependent on the pain of injection already described and to be independent of the level of the alcohol content of the blood. The pain and increase in pressure do not appear if the alcohol is administered in a 10 per cent solution or by mouth, although the curve for the subsequent alcohol content of the blood may attain a high level, depending on the dose.

The time of the beginning of the injection is noted as zero minutes, and in the course of the next three hours specimens of whole blood and cerebrospinal fluid

3. Gabbe, E.: Ueber den Gehalt des Blutes an Alkohol nach intravenöser Injektion desselben beim Menschen, Deutsches Arch. f. klin. Med. **122**:81, 1917.

4. Mehrtens, H. G., and Newman, H. W.: Alcohol Injected Intravenously: Its Penetration into the Cerebrospinal Fluid in Man, Arch. Neurol. & Psychiat. **30**:1092 (Nov.) 1933.

are taken synchronously at intervals of ten, twenty, thirty, forty, fifty, sixty, eighty, one hundred, one hundred and twenty, one hundred and fifty and one hundred and eighty minutes. The specimens are then analyzed for the alcohol content by the method described in paper I of this series.

The experiment was performed on twenty-eight subjects, consisting of ten heavy drinkers, eleven moderate drinkers and seven abstainers. Our basis in general for the selection of persons representing the different drinking habits is as follows: (*a*) Heavy drinkers are patients with alcoholism of such severity as to be directly responsible for their admission to the Boston Psychopathic Hospital; (*b*) moderate drinkers are persons (some of whom might ordinarily be classified as heavy drinkers) whose drinking habits bear no direct relation to their admis-

Average Concentration of Alcohol (Milligrams per Hundred Cubic Centimeters) of the Blood and Cerebrospinal Fluid Following Intravenous Injection of Alcohol

	Time After Injection, Min.											
	0	10	20	30	40	50	60	80	100	120	150	180
Heavy drinkers (10)												
Blood	4.5	132.3	95.0	73.0	66.9	62.9	58.8	54.2	49.8	44.9	39.6	33.4
Cerebrospinal fluid	4.3	13.2	25.3	37.2	45.3	50.3	53.1	55.5	55.6	54.8	52.1	46.5
Moderate drinkers (11)												
Blood	4.3	122.7	87.1	69.4	63.0	58.8	55.1	50.4	46.5	42.3	38.5	33.2
Cerebrospinal fluid	4.3	14.4	29.1	39.6	47.1	51.5	55.0	55.5	55.2	54.5	51.2	47.1
Abstainers (7)												
Blood	4.7	133.9	98.4	76.4	67.7	63.0	58.4	53.5	48.9	44.8	40.6	35.8
Cerebrospinal fluid	4.6	14.3	27.3	35.9	44.7	52.8	56.7	59.8	60.4	59.8	56.8	49.2
Clinical Group												
Without psychosis (7)												
Blood	5.0	138.4	103.1	74.3	67.9	64.7	59.9	55.2	50.8	45.4	40.8	34.0
Cerebrospinal fluid	4.6	11.2	21.8	31.1	37.7	42.7	47.0	52.9	54.4	55.3	53.2	47.6
With syphilis of central nervous system (7)												
Blood	4.3	123.5	88.4	72.0	63.3	57.8	53.3	48.1	43.6	39.9	35.7	29.4
Cerebrospinal fluid	4.4	13.6	27.6	36.6	43.9	49.2	51.6	53.9	54.6	54.0	51.4	43.6
With alcoholic psychosis (4)												
Blood	4.7	129.0	89.5	69.5	64.3	60.6	56.7	52.7	47.5	42.7	36.3	22.2
Cerebrospinal fluid	4.5	14.2	29.5	42.9	52.6	57.8	58.7	57.7	56.4	54.7	50.9	34.3
With schizophrenia (6)												
Blood	4.1	118.5	88.8	71.3	65.0	60.8	58.0	53.4	49.9	47.0	42.8	40.9
Cerebrospinal fluid	4.0	18.5	34.8	45.2	53.4	58.9	60.9	61.9	60.4	28.5	54.9	49.5

sion to the hospital, and (*c*) abstainers are persons who have never consumed alcohol. Clinically, the twenty-eight subjects can be divided into groups of six with schizophrenia, seven with syphilis of the central nervous system, four with alcoholic psychosis, two with manic-depressive psychosis (depressed) and two with psychoneurosis; seven of the subjects were without psychosis. Composite curves for any of the clinical groups or for the three groups classified on the basis of drinking habits (heavy and moderate drinkers and nondrinkers) can be constructed by averaging all the appropriate alcoholic concentrations for any given time and using the result as the average value for that time.

RESULTS

The accompanying table records the average concentration of alcohol of the blood and the cerebrospinal fluid for the four clinical groups

and for the three groups of drinkers and nondrinkers at the times indicated after administration; the results for the drinkers and abstainers are expressed graphically in the charts.

It is to be noted that the alcohol concentration of the blood decreases sharply during the first thirty minutes after injection and then gradually

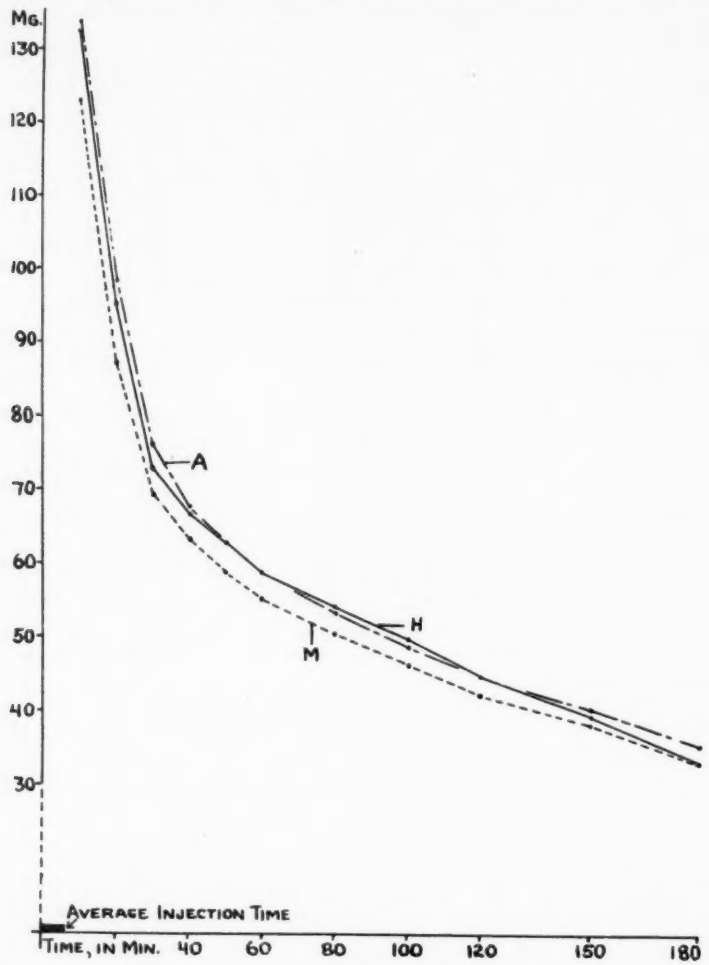

Chart 1.—Average alcohol content of the blood of ten heavy (*H*) and eleven moderate (*M*) drinkers and seven abstainers (*A*) after the intravenous injection of a standard dose. In this and in the accompanying chart the concentration of alcohol is expressed in milligrams per hundred cubic centimeters of blood or spinal fluid.

assumes a slower, more constant rate. The curves for the cerebrospinal fluid rise, cross those for the blood at the end of about sixty minutes and reach a maximal point in about eighty minutes; the concentration

in the cerebrospinal fluid decreases gradually after reaching this maximum and thereafter maintains a somewhat higher level than that of the alcohol content of the blood.

The composite curves for the alcohol content of the blood for the three groups of drinkers and nondrinkers seem to be essentially the same; certainly, the curves for the heavy drinkers and abstainers are identical, while the curve for the moderate drinkers runs parallel to the curves for the other groups at a slightly lower level. The composite curves for the alcohol content of the cerebrospinal fluid for the three groups are the same during the first hour after injection, and those

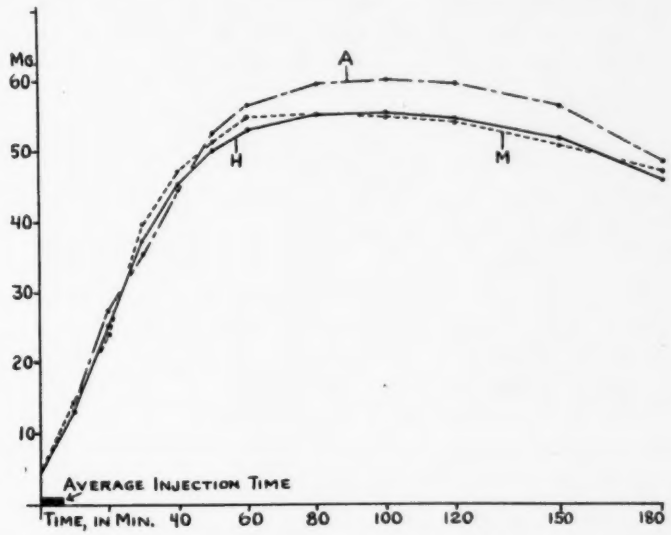

Chart 2.—Average alcohol content of the spinal fluid of ten heavy (*H*) and eleven moderate (*M*) drinkers and seven abstainers (*A*) following the intravenous injection of a standard dose.

for the heavy and moderate drinkers are identical throughout the three hours; however, the curve for the cerebrospinal fluid for the abstainers breaks away from the curves for the moderate and heavy drinkers at about the sixty minute point and maintains from then on a somewhat higher level than that of the two other curves. The significance of this apparently slightly greater passage of alcohol into the spinal fluid of abstainers, as obtained from the lumbar region, will be discussed later.

The composite curves for the four clinical groups (patients without psychosis and those with syphilis of the central nervous system, alcoholic psychosis and schizophrenia) seem to show no significant differences.

COMMENT AND CONCLUSION

In the light of the data already given, the following conclusions seem warranted:

After intravenous administration of alcohol the rate of its disappearance from the blood during the period studied (three hours) is the same for heavy and moderate drinkers and nondrinkers. That the curve for the moderate drinkers runs at a slightly lower level than the curves for the heavy drinkers and abstainers is probably due to the fact that the average time of injection for the group of moderate drinkers as a whole was somewhat shorter than that for the groups of heavy drinkers and abstainers; the average time of injection for the group of moderate drinkers was six and three-tenths minutes, for the heavy drinkers, seven and one-tenth minutes, and for the abstainers, six and nine-tenths minutes.

It is possible to point out the following main factors which determine the shape of the curves for the alcohol content of the blood: (*a*) dilution of the alcohol by the blood and equalization of the alcohol concentration of the blood throughout the circulatory system, (*b*) the passage of alcohol from the blood into the tissues and (*c*) elimination by excretion and possibly by oxidation. In the first part of the curve (from zero to thirty minutes) the alcohol concentration of the blood decreases rapidly owing to dilution by the blood, the rapid penetration of alcohol into the tissues (suggested by the sharp initial increase in the concentration of the cerebrospinal fluid) and elimination. As the alcohol concentration of the tissues approaches equilibrium with that of the blood, the curve for the blood flattens out and represents more nearly the slope for excretion (and possibly oxidation).

After intravenous administration alcohol seems to penetrate the cerebrospinal fluid of abstainers to a somewhat greater extent than that of moderate and heavy drinkers. The difference between the level reached by the concentration of alcohol in the spinal fluid of the abstainers on the one hand, and that of the concentration for the moderate and heavy drinkers on the other is not large, and therefore its actual significance is doubtful.

As was pointed out in paper I of this series, after the oral ingestion of alcohol no correlation could be demonstrated between the clinical diagnosis and the type of curve; this finding has been confirmed after the intravenous administration of alcohol.

On the basis of these conclusions it is possible to interpret more definitely and with greater assurance the findings after oral ingestion of alcohol, in which, in addition to the aforementioned factors, there is also the added factor of varying rates of absorption from the gastrointestinal tract. Since the curves for the blood after intravenous

administration are alike, this added factor must be responsible for the differences observed in the curves after oral administration.

As we have shown previously after oral ingestion, the alcohol concentration of the blood increases more rapidly, reaches a higher peak and decreases more quickly in heavy drinkers than in abstainers, with the values for moderate drinkers occupying an intermediate position. In the three curves the more rapid rise for heavy drinkers is associated with a higher peak and a more rapid decline, while the reverse in all three respects is true for abstainers. At the time the peak of concentration in the blood is reached the heavy drinker must have absorbed into the blood a greater portion of the oral dose than has the abstainer. Since the rate of disappearance from the blood up to this time was essentially the same for the three groups of drinkers and nondrinkers, it is evident that the essential and primary element in this situation is the rate of absorption from the gastro-intestinal tract: Given a faster rate of absorption there must inevitably follow a higher peak of concentration in the blood, and with a slower rate, a lower peak. The higher peak, in turn, contributes to a faster decline, owing partly to the greater penetration into the tissues with the higher alcohol concentration of the blood, as was pointed out in the consideration of the curves obtained after intravenous injections. As penetration into the tissues and absorption from the gastro-intestinal tract become more complete and less operative as direct factors, excretion and possibly oxidation become more and more the sole cause of the decrease in the alcohol concentration of the blood.

After the peaks are reached and the first rapid decrease in the concentration for heavy drinkers occurs the curves for the blood cross, and the curve for the heavy drinkers gradually assumes and maintains the lowest position. The amount of alcohol entering the blood from the gastro-intestinal tract is now smaller for the heavy drinkers than for the abstainers (because there is presumably less alcohol left in the gastro-intestinal tract of heavy drinkers), so that the rate of disappearance of alcohol from the blood continues to be somewhat greater for the heavy drinkers, although the concentrations in the blood are about the same for the three groups at this time. During this period (after from fifty to seventy minutes) the curves separate and then later (in from one hundred and twenty to one hundred and eighty minutes) seem to become essentially parallel, i. e., to show approximately the same rates of elimination.

From the curves for the blood obtained after oral administration in these experiments and from the investigations of others it is evident that at the end of three hours after drinking the heavy drinker has eliminated more alcohol from the blood than the abstainer; the chief

difference that has appeared between the curves for the groups during this period is the higher peak for the heavy drinker, due to more rapid absorption from the gastro-intestinal tract. Hence, we think that the rate of disappearance of alcohol from the blood at any given time must be proportional to the alcohol concentration of the blood at that time, so that the greater the concentration the more rapid the rate, at least within undetermined limits. That would seem to be the explanation of the prevailing opinion [5] that the drinker oxidizes alcohol faster than the nondrinker: In the drinker alcohol can be removed from the blood faster, because following oral ingestion the alcohol concentration of the blood reaches a higher level. That oxidation is the reaction involved we do not regard as proved. Our conclusion that habituated subjects absorb alcohol from the gastro-intestinal tract faster than nonhabituated ones confirms for man the findings made by Faure and Loewe [6] in rabbits after an oral dose of 3 cc. of absolute alcohol (in a 6 per cent solution) per kilogram of body weight. These authors, using four heavily habituated rabbits (for from three to eight months), six moderately habituated rabbits (for from thirty-three to eighty-two days) and twelve nonhabituated animals, found that on the average the alcohol concentration of the blood reached a higher peak and decreased to a lower level subsequently in the habituated than in the nonhabituated animals.

As far as the curves for the cerebrospinal fluid are concerned, we see no reason to alter the position taken in part I of this study, viz., that the shape and relation of these curves to those for the blood depend on a "diffusion lag" between the blood and the cerebrospinal fluid, the latter system acting as a "metabolically inert reservoir as far as alcohol is concerned." [7] It is tempting to assume that in the course of alcohol-

5. Emerson, H.: Alcohol and Man, New York, The Macmillan Company, 1932, pp. 5, 10, 130 and 201.

6. Faure, W., and Loewe, S.: Der Alkoholspiegel im Blute gewöhnter und ungewöhnter Kaninchen nach einem Probetrung, Biochem. Ztschr. **143**:47, 1923.

7. At the suggestion of Dr. Frank Fremont-Smith, we investigated the concentration of alcohol of blood plasma as compared to that of whole blood and were able to confirm the findings of Miles (J. Pharmacol. & Exper. Therap. **20**: 265, 1922), namely, that the alcohol concentration of the plasma is from 5 to 20 per cent greater than that of whole blood at any given time and that the curve for the alcohol content of the plasma runs approximately parallel to that for whole blood during the period studied (from ten to one hundred and eighty minutes after intravenous injection). These findings do not alter the concept of "diffusion lag," since the relative positions of the curves for the blood and spinal fluid are approximately the same whether whole blood or plasma is used for determinations of the blood. Furthermore, the application of Nicloux's hypothesis (Bull. Soc. chim. biol. **16**:330, 1934) that the water content of a tissue determines the amount

ism changes in the sense of decreasing permeability to alcohol occur in the hemato-encephalic barrier and that the interplay of this decreased permeability between the blood and spinal fluid systems and the proved increased gastro-intestinal permeability provides a physiologic basis for tolerance; however, we do not think that such a conclusion can be drawn from our data.

SUMMARY

Standard doses of alcohol (0.6 cc. of absolute alcohol per kilogram of body weight) were administered intravenously to twenty-eight subjects, and synchronous curves for the alcohol content of the blood and cerebrospinal fluid were constructed for a period of three hours after injection.

The experimental subjects consisted of six patients with schizophrenia, seven with syphilis of the central nervous system, four with alcoholic psychosis and two with psychoneurotic conditions; seven of the subjects were without psychosis. According to their drinking habits the subjects were divided into groups of ten heavy and eleven moderate drinkers and seven abstainers.

Comparison of the composite graphs for the different groups led to the following conclusions:

1. After intravenous administration alcohol disappears from the blood at the same rate in heavy and moderate drinkers and abstainers.

2. The alcohol concentration apparently reaches and maintains a slightly higher level in the cerebrospinal fluid of abstainers than in that of drinkers, but the significance of this is doubtful.

3. The clinical picture bears no direct relation to the shape of the curves, but the general drinking habits of each group seem rather to determine the shape of the composite curves.

The implications of these conclusions in interpreting the curves for the alcohol content of the blood and cerebrospinal fluid after oral administration are pointed out.

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of alcohol it will absorb does not bring the two curves together. In actual experiments on determinations of the water content of the plasma and spinal fluid there is considerably more alcohol in the spinal fluid at any given time (after the curve for spinal fluid has crossed that for the blood) than would be expected. These considerations are of great importance in an attempt to interpret the slight differences in the curves for the spinal fluid for the different types of drinkers. Such differences may be merely reflections by the spinal fluid of an altered partition of alcohol between the cells of the blood and the blood plasma in chronic alcoholism rather than represent a changed permeability of the barrier between the blood and the spinal fluid.

Clinical Notes

PERNICIOUS ANEMIA AND COMBINED SYSTEM DISEASE WITH DIABETES MELLITUS AND PARKINSONIAN SYNDROME

Report of a Case

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ST. LOUIS

This case is reported because of its uniqueness and because of the emphasis laid on an important principle in the economy of the nervous system. That is, when the balance between two opposing systems is interfered with by disease, the clinical picture is so modified that it may lose one or several of its characteristic qualities. In this case a parkinsonian syndrome occurred without rigidity of muscles and without the characteristic masklike facies. The presence of lesions in the posterior column as a result of pernicious anemia so decreased the tonic qualities of the neuromuscular system that although a lesion was postulated in the striate system no rigidity was found and the muscles were hypotonic.

From the series reported by Ahrens,[1] Weil,[2] Wilkinson[3] and Woltman[4] and the recent article by Goldhamer, Bethell, Isaacs and Sturgis,[5] it is agreed that about 80 to 90 per cent of all patients with pernicious anemia present demonstrable signs and symptoms of involvement of the spinal cord. Pathologically there is demyelinization in the posterior columns, in the anterolateral columns and in the pyramidal tracts. Further discussion of this matter is outside the scope of

From the Department of Internal Medicine and Neuropsychiatry, Washington University School of Medicine, and Barnes Hospital.

1. Ahrens, Richard: Neurologic Aspects of Primary Anemia, Arch. Neurol. & Psychiat. **28**:92 (July) 1932.

2. Weil, Arthur, and Davison, Charles: Changes in the Spinal Cord in Anemia: A Clinicomicroscopic Study, Arch. Neurol. & Psychiat. **22**:966 (Nov.) 1929.

3. Wilkinson, John F.: Diseases Associated with Pernicious Anemia, Quart. J. Med. **2**:281, 1933.

4. Woltman, H. W.: The Nervous Symptoms in Pernicious Anemia: An Analysis of One Hundred and Fifty Cases, Am. J. M. Sc. **157**:400, 1919.

5. Goldhamer, S. M.; Bethell, F. H., Isaacs, Raphael, and Sturgis, Cyrus C.: The Occurrence and Treatment of Neurologic Changes in Pernicious Anemia, J. A. M. A. **103**:1663 (Dec. 1) 1934.

this paper. Barrett [6] and Woltman [7] showed that the frequent occurrence of paranoid psychosis in cases of pernicious anemia can be correlated pathologically with diffuse cortical degeneration similar to that in the cord in 80 per cent of the brains examined.

The coincidence of diabetes and pernicious anemia is not rare. Root [8] reported 79 cases, in which he noted that the response to liver therapy, as measured by the rise in the reticulocyte count, is about half that in cases of uncomplicated anemia.

The association of Parkinson's disease with pernicious anemia is, however, exceedingly rare. We have studied 1,493 cases of pernicious anemia in the literature, and only in Wilkinson's series [3] was an instance found, which, unfortunately, was not described.

Paviot and Dechaume [9] reported the autopsy in a case of pernicious anemia in which there was bilateral degeneration of the globus pallidus, similar to that in the cord, but there was no tremor. Of Woltman's [7] series of 7 brains from persons with pernicious anemia, one showed a degenerative lesion in one caudate nucleus, but there had been no tremor. In another paper by the same author [4] a case of pernicious anemia with choreiform movements is mentioned in a series of 150 cases of that disease.

No further mention of Parkinson's disease with pernicious anemia was found in the literature of the last twenty-five years. Neither Castle nor Weiss,[10] at the Thorndike Memorial Laboratory of the Boston City Hospital, has ever observed this complication.

REPORT OF CASE

D. S., an American widow aged 69, was admitted to Dr. David Barr's medical service of the Barnes Hospital on Nov. 8, 1934, and after a short period was transferred to the neurologic service. She entered the hospital because of extreme weakness, numbness of the feet and hands and trembling of the hands of about nine months' duration. The significant fact in the past history was that throughout life she had suffered from intermittent diarrhea, brought on by eating meat. As a result she had been on a practically meat-free diet for the past sixty years. One sister had diabetes. Four years before, she consulted a physician on account of loss of strength, polyuria and polydipsia. She was found to have diabetes. After an unsuccessful trial of a diet therapy, she was sent to the medical service of the Barnes Hospital on June 12, 1931. At that time examination of the blood, including a red cell count, estimation of hemoglobin and smear, gave normal results. There was no evidence of disease of the nervous system, but a smooth tongue was noted. The diabetes responded readily to treatment, and after a week the patient was discharged on a diet of carbohydrate 85 Gm., fat 130 Gm. and protein 45 Gm. with

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6. Barrett, A. M.: Mental Disorders of Pernicious Anemia, Am. J. Insan. **69**:1063, 1913.

7. Woltman, H. W.: Brain Changes and Pernicious Anemia, Arch. Int. Med. **21**:791 (June) 1918.

8. Root, Howard F.: New Cases of Combined Pernicious Anemia and Diabetes, New England J. Med. **208**:819 (April 20) 1933.

9. Paviot, J., and Dechaume, J.: Considérations sur un syndrome neuro-anémique avec lésions diencéphaliques, chez une tuberculeuse pulmonaire non évolutive, Bull. Acad. de méd., Paris **109**:102, 1933.

10. Castle, W. B., and Weiss, Soma: Personal communication to the author.

25 units of insulin daily in doses of 10, 5 and 10 units. She followed this diet and took insulin for a year and then became careless about both.

About two years ago she noted gradual loss of both appetite and strength, with periods of lassitude and fatigue, which were particularly marked in the winter months. Eleven months before admission to the hospital she felt for the first time a burning sensation in the right hand, which spread to the left hand in a few weeks. Nine months before entrance she complained of trembling of the right hand. Two weeks later, both hands were involved. The trembling increased on excitement and at the time of the observation and examination. Seven months before entry the feet felt numb, distant and awkward, and there was a marked increase in weakness and lassitude. A month later she entered a hospital in Illinois, where the diabetes was regulated. In the abstract of the record from that hospital no note was made of the condition of the blood, of a neurologic examination or of the presence of tremor. After a week she returned home, at which time paresthesia, numbness, difficulty in walking and general weakness all increased in severity. There was at no time any loss of control of the sphincters or numbness in that region.

Physical Examination.—There was evident loss of strength and weight. The skin was pale, yellowish and dry. The patient lay in bed, showing a well marked, rather typical parkinsonian tremor of the hands and a to-and-fro nodding of the head. There was no parkinsonian mask and only a slight slumping forward in bed. The pupils were normal; the fundi showed arteriosclerosis; there was a cataract in the left eye. The cranial nerves, except for some loss of taste, were normal. The tongue was typically red, smooth and atrophic.

The heart and lungs were normal. The blood pressure was 110 systolic and 70 diastolic. The abdomen was normal except that the smooth edge of the liver was just palpable. Vaginal examination gave normal results. Rectal examination revealed good sphincter tone. The extremities presented some senile wasting, with peripheral arteriosclerosis, but pulsation was obtained in the dorsalis pedis artery of each foot. The reflexes were hyperactive, the right greater than the left, without clonus. The Babinski sign was present on the right, and both abdominal reflexes were absent (flabby musculature). Vibratory sensation was quantitatively present, 25 per cent normal at the mastoids and 12 per cent at the malleoli; loss was most marked over the right side. The sense of position was diminished in the feet. There was hypesthesia to pin prick in stocking and glove distribution and anesthesia to cotton wool over the same area. There was some dissociation of heat and cold over both feet. A typical parkinsonian rolling tremor was present in the hands, and it disappeared entirely when the patient dozed or was asleep. As the tremor of the hands increased from excitement or fatigue, there was more movement of the head and legs. There was absolutely no muscular rigidity anywhere; in fact, there was hypotonia in the muscles of the legs and arms.

Laboratory Findings.—The urine contained sugar and albumin; the specific gravity was 1.02; there was no sediment. The sugar content of the blood (after fasting) was 198 mg. per hundred cubic centimeters; the nonprotein nitrogen content, 53 mg. The Kahn test of the blood was negative. Gastric analysis, even after the injection of 1 cc. of histamine, showed no free acid and no occult blood. The sugar tolerance showed a typical diabetic curve. The basal metabolic rate was minus 2. The blood contained 1,800,000 red cells per cubic millimeter, 40 per cent hemoglobin, 4,000 white cells and 120,000 platelets. The blood smear con-

tained 1.6 per cent reticulocytes, 56 per cent polymorphonuclear leukocytes and 44 per cent lymphocytes; there were anisocytosis, poikilocytosis and an abundance of macrocytes.

Course.—The patient was treated with injections of 3 cc. of a solution of liver extract intramuscularly twice a week.[11] In ten days the reticulocytes reached 3.5 per cent, and the red cells, 2,000,000; in twenty days the reticulocyte count was 7.7 per cent and the red cell count, 2,800,000, with hemoglobin 47 per cent. At this point the patient looked and felt better; she showed improvement in appetite and interest in the surroundings. There was, however, no change in the tremor or in the results of a neurologic examination.

The patient was discharged on Dec. 11, 1934, with her condition improved. At that time the red blood cell count was 3,750,000; the hemoglobin content, 80 per cent (Sahli), and the reticulocyte count, 7.1 per cent. The diagnosis at the time of the patient's discharge was pernicious anemia and combined system disease, with parkinsonian syndrome.

COMMENT

The appearance of the parkinsonian syndrome in the course of pernicious anemia is so rare that some explanation is necessary. There is no reason per se that Parkinson's disease should not develop in a person with pernicious anemia as a mere coincidence. The two conditions, then, might be said to have no common causation and to be linked together simply in time. Leaving out the parkinsonian syndrome which results from various types of encephalitis, it occurs late in the fifth decade and onward. Pernicious anemia is more common in the fourth decade. This fact would tend slightly to diminish the probability of coincidence in the occurrence of these two diseases together. That the occurrence of Parkinson's disease and pernicious anemia together is almost unknown in the literature suggests that the fortuitous development of these two diseases in one person might not be explained by the time element alone. Rather it would seem that when these two diseases do occur it is as a result of something other than pure coincidence. In the case here described, the fact that the parkinsonian syndrome was not complete, that it lacked rigidity, which is perhaps the fundamental symptomatic expression of the lenticulostriate situation of the disease process, supports the view of a common cause and weakens the importance of coincidence. The complete clinical picture in this case points to a lesion associated with the essential disease in this particular patient, that is, pernicious anemia. In this case the progress of events tends to link these two conditions together as having a common etiology. The localization of the process in the lenticulostriate region is the coincidental factor and not the presence of the two conditions in the same person. The factor in pernicious anemia that causes the well known changes in the posterior and lateral portions of the cord has not been identified, nor is the actual process which takes place fully understood. The microscopic appearance of sections of the spinal cord gives no indication of where the process is primarily located or on what its progress depends. The changes in the spinal cord which are found in the posterior and lateral columns are similar to the pathologic changes in the brain as a whole.

In order to interpret the changes in the lenticulostriate region which are assumed to have taken place in this case, a different kind of mechanism must be predicated that would be accounted for by the anemia itself. The parkinsonian syndrome in this case cannot be differentiated from that in ordinary parkinsonian

11. Lederle's solution of liver extract was used.

disease due to whatever cause, except by the absence of rigidity. The symptoms suggest a degeneration in the cells composing the nucleus itself and show essentially the same unchangeableness and progressiveness as do the symptoms produced by posterior and lateral changes in the column. Therefore, one might hazard that the same factor that causes changes in the spinal cord is active in producing the changes in the cells of the lenticulostriate region. The absence of muscular rigidity and the usually accompanying lenticulostriate syndrome should be interpreted. Two explanations are possible. One is that localization of the lesions in both lenticulostriate regions is limited to the neostriatum and that the putamen has escaped entirely. This would account for the prevalence of movement instead of rigidity or plastic posture. There are many objections to this interpretation; chiefly, it would be difficult to explain why the factor of pernicious anemia should select only one part of the lenticulostriate mechanism and leave the rest untouched. If the theory of system location is valid, as is the case in the spinal cord, then the total function of the lenticulostriate nucleus should be involved. A much more reasonable explanation appears to be that the whole of the lenticulostriate region is involved in this process and that the hypotonia replacing the rigid concomitant of the neuromuscular system is due to the effect on muscle tonus of the involvement of the posterior column. That is to say, before the lenticulostriate region became affected by the process there was already a well developed progressive state of hypotonia, so that when the lenticulostriate region began to show by its symptoms that it also was attacked by the etiologic factor in pernicious anemia, a degree of hypotonia had been established which could not be overcome by the development of the rigidity in the lesion affecting the region near and around the putamen. This would appear to be the most reasonable explanation of this curious and unusual combination of pernicious anemia and parkinsonian syndrome, without rigidity and with hypotonia. It is for this reason chiefly that this case is reported, because it presents a physiologic problem of the most unusual kind and may open a way for experimental research and open the question of the physiologic balance between two opposing systems in the spinal cord and brain.

FAMILY PERIODIC PARALYSIS IN A GIRL AGED SEVENTEEN

J. A. BENDER, M.D., CLEVELAND

Family periodic paralysis is a rare disease of unknown etiology. Reports of cases have appeared in the literature from time to time since Hartwig in 1874 published the first report of an undoubted case of the disease under the title "Intermittent Spinal Paralysis." Singer and Goodbody [1] in 1901 summed up the main clinical features of the condition as follows: "Periodic attacks of flaccid paralysis in an otherwise healthy individual, of varying duration from 5 or 6 to 72 hours, during which there is a gradual and progressive onset, leading in complete attacks to absolute paralysis of all four extremities, neck, and trunk but not affecting as a rule the muscles supplied by the cranial nerves. Proceeding pari passu with this loss of power there is loss of muscular excitability to electricity and percussion and abolition of all reflexes in the affected parts. There is never at any time any loss of consciousness, or impairment of mental function, nor any demonstrable change in any afferent path." Most of the earlier cases described were considered to be familial. Recent descriptions have included many cases in which there was no familial background but in which the clinical features were similar to those in cases described as familial.

I have had the opportunity to observe a case of periodic paralysis over a period of more than two years, during which time major attacks of paralysis have ceased to occur. The only remaining difficulty is weakness of the legs and a rare abortive attack.

Because the disease is of such rarity,[2] I thought it worth while to add the report of this case to those previously published.

REPORT OF CASE

History.[3]—C. S., an American schoolgirl aged 17, was admitted to the outpatient department of the Lakeside Hospital on Sept. 10, 1932, complaining of periodic attacks of paralysis and weakness of the legs, which were exaggerated during the menstrual periods. For an indefinite period preceding the first attack of paralysis the patient had experienced weakness of the legs. This weakness was such that on one or two occasions she had fallen while walking on the street and while walking about the house. Climbing stairs had been most difficult.

The illness had begun four years previously, at the age of 13, at the menarche, when the patient awoke one night from a sound sleep to find herself unable to move. She was unable to turn over in bed. This attack lasted about twenty-four hours

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From the Department of Medicine, Western Reserve University, and the Medical Service, Lakeside Hospital.

1. Singer, H. D., and Goodbody, F. W.: A Case of Family Periodic Paralysis, with a Critical Digest of the Literature, Brain **24**:257, 1901.

2. This was the first case observed in the Lakeside Hospital in 162,016 admissions.

3. The patient was presented before the Cleveland Neurological Society, Cleveland, Nov. 9, 1932.

and was followed by gradual return of strength in the extremities during a period of from thirty-six to forty-eight hours. During this attack the limbs were completely flaccid and easily movable by any one else. Since the first attack, the patient had had eleven major attacks, most of them coming on at night, so that she would awake and find herself unable to move in bed. While they occurred more frequently at night, she also had attacks during the day. For example, one early attack occurred in an automobile during the course of a trip between neighboring towns. There was no history of periodic paralysis in the family, nor was there a history of any paroxysmal disorder, such as epilepsy or migraine.

The initial attack of paralysis came on shortly after the second menstrual period was due. Later attacks did not coincide with the periods, but the patient observed that the persistent weakness of the legs was exaggerated about two days prior to the onset of menstruation. There had not been a disturbance in the menstrual cycle save for the failure to menstruate at the time the second period was due. The periods otherwise had been normal and had not been accompanied by pain or any other abnormality. They appeared every twenty-eight days and were of five days' duration.

On the first visit to the outpatient department the mother was instructed to bring the patient to the hospital at the onset of the next attack. Accordingly, on Oct. 14 at 7:30 p. m., the patient was admitted to the hospital, and the following history was obtained: At about 1:30 a. m. on the day of the patient's admission to the hospital she awoke and found herself unable to turn in bed. She called her mother, who found the extremities completely flaccid. There was no disturbance of speech, paralysis of the muscles of the face or sphincter disturbance. On the morning of admission to the hospital the patient was placed on a couch, where she rested most of the day. She was nauseated and vomited several times with some difficulty, aided by salt water. (In most of the eleven attacks she had been nauseated and had vomited.) She did not experience pain, twitching or paresthesia; she was sensitive to pain stimuli and was able to distinguish between heat and cold.

Physical Examination.—The patient was a rather slender, poorly developed girl lying quietly in bed, unable to move her extremities. In physical and emotional development she presented the appearance of a girl somewhat younger than her stated age of 17. Mentally, she was bright and intelligent but not very cheerful. The pupils were equal and regular and reacted to light and in accommodation. There was no nystagmus or exophthalmos. The fundi were normal, and vision was good. There was no facial asymmetry and no involvement of the cranial nerves. The tongue protruded in the midline. There was no tremor. The thyroid was not enlarged. The lungs were normal. There was a loud, blowing, systolic murmur at the apex. The cardiac borders were within normal limits. The rhythm was regular; the rate was 120 per minute. The blood pressure was 125 systolic and 75 diastolic. The extremities were entirely flaccid, and the patient was unable to move them. All reflexes were absent, both superficial and deep. No fibrillations were detected. There was no hypotonicity of the muscles. Sensory examination gave normal results. There was neither patellar nor ankle clonus, nor were there any pathologic toe signs. There were no signs of extrapyramidal involvement, such as tremors, twitching or rigidity.

The sympathetic system showed no obvious change; there were no vasomotor or sweating abnormalities. The hands were of normal color, warmth and dryness.

By the following day, thirty-six hours after the onset of the attack, the patient was able to move the extremities, but there remained a marked residual weakness.

All reflexes had returned but were greatly diminished. The patient was under observation in the hospital for fifteen days, during which time a major attack did not occur.

Laboratory Studies.—The urine was normal. The red blood cell count was 4,240,000, with a 73 per cent concentration of hemoglobin. There were 6,650 white blood cells, with 68 per cent polymorphonuclears, 26 per cent lymphocytes, 4 per cent mononuclears and 2 per cent eosinophils. The Wassermann reaction was negative. Examination of the spinal fluid gave normal results. The sugar content of the blood after fasting was 80 mg. per hundred cubic centimeters; the cholesterol was 119 mg.; the serum calcium was 11.1 mg., and the urea nitrogen and creatinine were within normal limits. The basal metabolic rate was minus 2 and minus 5 on two occasions. Galvanic stimulation of the muscles of the legs was not carried out until several days after the subsidence of the attack, and at that time they showed a lessened response. There was no beginning reaction of degeneration.

Course.—The patient was discharged from the hospital on October 29, and was observed at frequent intervals in the outpatient department. During this period she did not have a major attack of paralysis, though she complained of a persistent weakness of her legs.

Because of the reported exaggeration of weakness in the legs about two days before the onset of a menstrual period and with the thought that perhaps there was some dysfunction of the ovaries, she was given ovarian therapy, a 5 grain (0.325 Gm.) tablet of the dried residue (equivalent to 30 grains [1.95 Gm.] of the whole gland) being administered three times daily.[4]

On November 25 the patient complained that the weakness in the legs had been more marked than previously. She had tried to dance and was able to do so only a short time. Walking continued to be difficult, especially on climbing stairs. On this visit strychnine sulphate, 1/60 grain (0.001 Gm.) three times a day, was prescribed, in addition to ovarian substance.

During the next ten months the patient made six visits to the outpatient department, usually reporting some slight improvement and no attack of paralysis.

On Sept. 23, 1933 she was again having difficulty in climbing stairs and felt that strength in the legs was not as great as before. On examination at this visit, it was noted that there was a marked diminution in the intensity of the systolic murmur heard at the apex as compared with that heard at the time of the attack in the previous October.

Westphal[5] was the first to observe any change in the condition of the heart during an attack of periodic paralysis. He noted slight temporary enlargement. Goldflam[6] and Mitchell[7] described systolic murmurs without enlargement of the area of cardiac dulness. According to Singer and Goodbody,[1] the change consists in dilatation, with or without definite regurgitation through the mitral valve.

The patient reported on December 2 that she was feeling better than at any time in recent months. The strength in the legs was improving. She had started to

4. Lederle's ovarian substance was used.

5. Westphal, C.: Ueber einen merkwürdigen Fall von periodischer Lähmung aller vier Extremitäten, mit gleichzeitigem Erlöschen der elektrischen Erregbarkeit während der Lähmung, Berl. klin. Wchnschr. **32**:489, 1885.

6. Goldflam, S.: Ueber eine eigentümliche Form von periodischer familiärer, wahrscheinlich auto-intoxicatorischer Paralyse, Wien. med. Presse **31**:1418, 1890; Ztschr. f. klin. Med. (supp.) **19**:240, 1891.

7. Mitchell, J. K.: A Study of a Case of Family Periodic Paralysis, Am. J. M. Sc. **118**:513, 1899.

attend night school and was taking a moderate amount of exercise daily. On Jan. 31, 1934, and again on April 17 she reported continued improvement. She was last seen on Dec. 17, 1934, at which time she still had residual weakness of the legs on climbing stairs but was otherwise well.

At the time of writing the patient has not had an attack of paralysis since she was discharged from the hospital twenty-eight months ago.

COMMENT

Various theories have been propounded to explain the pathogenesis of this condition. Hartwig assumed that the condition was due to hyperemia of the spinal cord, with temporary increase of the serous exudation. Westphal [5] first suggested that the disease was due to some form of toxemia, and Goldflam [6] suggested that the toxemia was of the nature of an auto-intoxicant. In attempts to discover this toxin, detailed analyses were made by various observers of the blood, the urine and the feces. These analyses were made both during attacks of paralysis and in the intervals between attacks. No convincing evidence that such a toxin exists was found in any of these studies. Among other things, malaria, scarlet fever, heredity and physical overexertion have been considered as etiologic factors. None of these views have been adequately confirmed by experimental investigation.

In 1926 Shinosaki [8] published experimental evidence to show the relationship of family periodic paralysis to disturbances in function of the glands of internal secretion.

Five years later, in 1931, Dunlap and Kepler [9] reported four cases in which the occurrence of periodic paralysis was associated with hyperthyroidism and "alleviation of the state of hyperthyroidism was followed by disappearance of the recurring paralytic attacks."

In 1932 Morrison and Levy [10] reported one case of periodic paralysis associated with hyperthyroidism. Following thyroidectomy the attacks of paralysis diminished in intensity and frequency. These authors cited evidence from the work of Shinosaki to support the theory that periodic paralysis is the result of metabolic imbalance.

They stated further: "The results of carbohydrate variation, the blood sugar observations, and the effect of parathyroid preparations all give evidence, not by any means conclusive, that favors a theory of polyglandular disease rather than other theories, such as Schmidt's attempt to bring the disease in relation to a local ischemia of small arteries in muscle, or Lundborg's theory that the disease is due to hyperfunction of the parathyroid glands alone."

In the light of Shinosaki's work on the endocrine glands and their relation to periodic attacks of paralysis, I have thought that possibly there might be some relation between an ovarian dysfunction and the attacks of paralysis in my patient. The fact that the weakness of the legs was exaggerated just before the onset of a menstrual period may lend suggestive support to such a supposition. Whether

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8. Shinosaki, T.: Klinische Studien über die periodische Extremitätenlähmung, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:564, 1926.

9. Dunlap, H. F., and Kepler, E. J.: Occurrence of Periodic Paralysis in the Course of Exophthalmic Goitre, Proc. Staff Meet., Mayo Clin. **6**:*272* (May 6) 1931.

10. Morrison, S., and Levy, M.: The Thyroid Factor in Family Periodic Paralysis, Arch. Neurol. & Psychiat. **28**:386 (Aug.) 1932.

the ovarian substance played any great part in the cessation of the attacks is a question which I cannot now decide.

My case becomes of interest primarily because the major attacks of paralysis have ceased completely up to the time of writing, and the patient has been transformed from a semi-invalid to a girl with a fairly active interest in the affairs of her home and her friends. She has begun to go to night school and has been taking dancing and swimming lessons.

The etiology of the condition continues to remain obscure. The work of Shinosaki has thrown new light on the subject and has opened new avenues of thought, which may encourage further investigation in the study of the glands of internal secretion as a possible solution to this mystery.

SUMMARY

A case of periodic paralysis is reported in which eleven major attacks occurred during four years, the first attack coming with the menarche. The major attacks have completely disappeared, and during a part of the period in which no attacks have occurred the patient has been receiving ovarian therapy.

ASYMMETRY: UNILATERAL ATROPHY AND FACIAL HYPERTROPHY

Report of Cases

MABEL G. MASTEN, M.D., MADISON, WIS.

It is common knowledge that asymmetry is a constant feature of human development. However, gross asymmetry which is at once discernible, even if of one part, is rare, and a decided inequality of the two halves of the body constitutes the rarest of developmental anomalies, according to Halperin.[1] It is estimated that the number of cases of complete unilateral atrophy reported is less than twenty-five, while seventy-two cases of hemiphypertrophy have been reported.

Hemiatrophy, first described by Broca[2] in 1859, may be of various types, the commonest being facial atrophy. Less common are the crossed (the face involved on one side and the body on the opposite side) and the complete unilateral type. Many theories concerning the etiology have been developed, none of which is wholly satisfactory. It is my purpose in this paper not to present these theories but to present clinical data that may be helpful later in crystallizing ideas concerning the cause. Thus far only one case has been reported of complete hemiatrophy in which autopsy has been performed. Steven[3] in 1898 reported the case of a woman, aged 26, with total hemiatrophy associated with scleroderma. The cerebral cortex on the left was thinner than that on the right. There was diminution of the number of cells of the right anterior horn of the spinal cord, with signs of degeneration. There were no such changes in the pons and the medulla. Three cases of atrophy limited to the face have been studied pathologically (Mendel, Loebl and Wiesel and Grabs[4]). The examinations in these cases were limited, interest being centered on the gasserian ganglion and its branches and the brain receiving no consideration except in one case in which the brain stem from the hypoglossal to the oculomotor nuclei was serially sectioned and revealed no pathologic change. The etiology is speculative, but it seems logical to implicate visceral centers in the diencephalon. Certainly peripheral vegetative pathologic changes will not explain complete unilateral atrophy, and partial atrophy is to be looked on as a more circumscribed defect in the visceral centers or their central pathways.

Read before the Chicago Neurological Society, March 21, 1935.

From the department of neuropsychiatry, University of Wisconsin Medical School.

1. Halperin, G.: Normal Asymmetry and Unilateral Hypertrophy, Arch. Int. Med. **48**:676 (Oct.) 1931.

2. Broca, Paul: Angeboren Asymmetrie der beiden Körperhälften, Jahresb. ü. d. Leistung. d. ges. Med. **1**:6, 1859.

3. Steven, J. L.: Case of Scleroderma Adultorum, Glasgow M. J. **1**:401, 1898.

4. Grabs, cited by Archambault, L., and Fromm, N. K.: Progressive Facial Atrophy, Arch. Neurol. & Psychiat. **27**:529 (March) 1933.

REPORT OF CASES

A case of unilateral atrophy is reported here, which is more complete in details than previously reported cases.

CASE 1.—Elizabeth, aged 20, was the eighth child of Croatian parents. The mother's health was good throughout pregnancy, and delivery of the 4 pound (1,814.3 Gm.) baby was uncomplicated. Asymmetry was noted at birth, the left leg being 2 inches (5 cm.) shorter than the right and the left arm smaller than the right. Nails were present on the right hand and foot and were absent on the

Fig. 1 (case 1).—Photograph of the patient, showing left hemiatrophy

left. The child did not walk and talk until the age of 2½; when she entered school at 6 it was noted that sight and hearing were impaired on the left side. The patient remained in school until the age of 17, when she withdrew from the eighth grade. Menstruation began at 12; the first three periods were at twenty-eight day intervals, but after that the menses occurred from two weeks to seven months apart; the flow, which varied from three to seven days, was excessive. For the previous four or five years the patient had always been tired. Hearing and vision had become more and more impaired.

The pertinent observations were: The left arm and leg were shorter and the circumferences were reduced on the left (fig. 2). The left eyebrow was scantier

and the arch shorter and the left ear was smaller and at a higher level than those on the right side. The entire left side of the face was smaller than that on the right, with a smaller aperture between the open eyelids on the left and smaller orbits and sinuses. The pupil of the left eye was smaller than that of the right eye, and the jaw, tongue and palate were smaller on the left than on the right side. The left third molar was impacted, while that on the right was in good alinement. The left breast and nipple were smaller than those on the right. The left half of the thorax and abdomen was pigmented. The pelvis was tilted, with

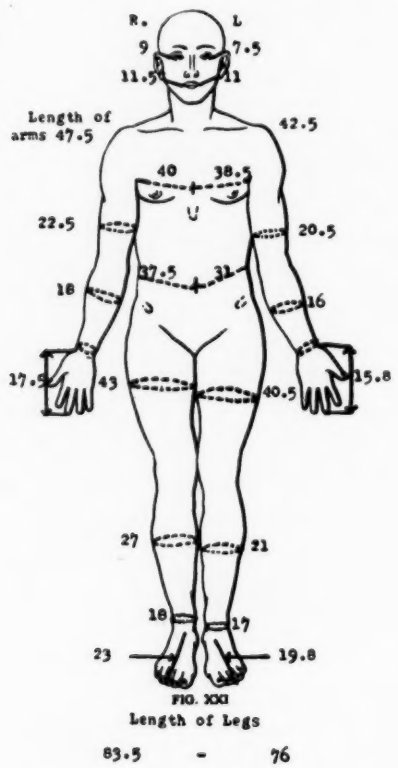

Fig. 2 (case 1).—Chart showing uniform reduction in the measurements for length and girth of the left side.

scoliosis compensating for the short left leg. The left labia pudendi were smaller than the right; there was less pubic hair on the left, and there was almost no hair in the left axilla. The nails on the left hand and foot were rudimentary and defective.

Vision in the left eye was 20/100, and in the right eye 20/20. There was deafness on the left. The left vocal cord was fixed in adduction, and there was an infantile epiglottis. The heart presented a functional murmur. A roentgenogram of the chest revealed fulness of the pulmonic arch. There was no free acid in the gastric contents after an Ewald test meal, but acid was present in normal

amounts after the administration of histamine. Otherwise the gastro-intestinal studies gave normal results. Sweating, both spontaneous and induced by pilocarpine, was diminished on the left. The uterus was infantile.

Roentgenograms showed the long bones to be shorter and smaller on the left than on the right but with normal architecture. The skull showed a thinner calvarium on the left, but that on the right was unusually thick and sclerotic. There were a defect in the neural arch of the fifth lumbar vertebra and spina bifida at the first lumbar vertebra. The pelvic bone on the left was reduced in size.

Biopsy of a specimen of skin from each side of the abdomen revealed all the structures on the left to be reduced in size and number, including the arteries

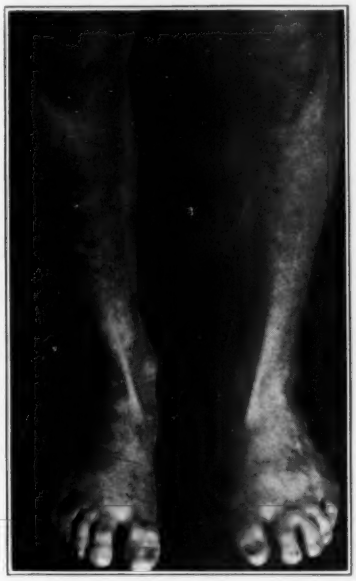

Fig. 3 (case 1).—Photograph showing defective nails on the left foot.

and the nerves; the amount of pigment was increased in the basal cell layer on the left. The striking feature was the reduction in the size and number of nerves.

Physical and mental inferiority were noted (height, 4 feet and 10½ inches [148 cm.]; weight, 96 pounds [43.5 Kg.]; intelligence quotient, 67). Neurologic examination revealed normal muscle tone and function as well as normal reflexes.

An encephalogram disclosed enlarged ventricles and general reduction of air in the cortex, which was marked on the right. No attempt has been made to correlate these observations with the clinical findings. Sclerosis of the mastoid cells was visible (fig. 5).

The following case is one of atrophy limited to the face and upper half of the trunk on the left side:

Case 2.—Helen B., aged 15, had always been frail, having had dietary difficulties in the first year and many illnesses, including influenza during the epidemic

of 1919. Walking and talking were delayed until the age of 3. The patient menstruated at the age of 11, but the menstruation had always been irregular. She was easily fatigued and was dyspneic on walking or after any sustained effort. The teeth had always been of poor structure, dentition being delayed until 1 year of age; the first teeth decayed rapidly, and recently the upper teeth had been extracted because of decay. Three years previous to examination, within a year's time, the patient had three spells of numbness lasting one-half hour and involving the left side of the body; the first was limited to the face, tongue

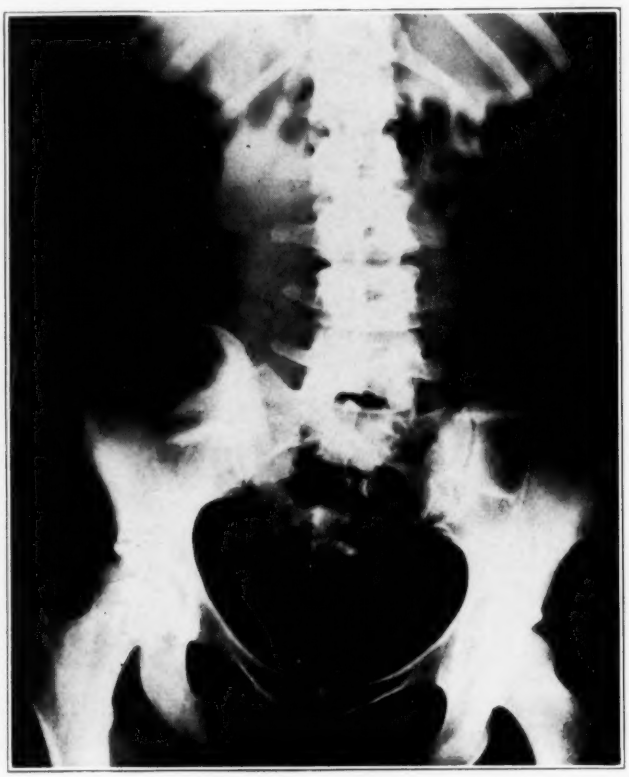

Fig. 4 (case 1).—Roentgenogram showing normal bone architecture but dissimilarity in size, with compensatory tilting. Note spina bifida at the first lumbar vertebra and a defect in the neural arch at the fifth lumbar vertebra.

and left arm, while the others involved the entire left side. There was no loss of consciousness, nor was there motor weakness. There was some difference of opinion over the appearance of atrophy. The mother had become aware of it at puberty when the patient's left breast failed to develop as well as the right. The physician who referred her to me called the maldevelopment a congenital deformity. The patient stated that the left side of the face and thorax had been smaller than the right as long as she could remember.

The essential observations were: The height was 5 feet and 1½ inches (156 cm.); the weight, 116 pounds (52.6 Kg.), and the intelligence quotient, 81. Posture was poor. There was facial asymmetry, although it was difficult to decide from inspection which side was less developed, the patient insisting that it was the left side. Roentgenograms of the facial bones revealed those on the left to be less developed than those on the right. The entire thorax below the clavicle was less well developed on the left; the measurements from the midsternum to the center of the vertebral column, taken above and below the breasts and at the nipple, being 3 cm. less on the left than on the right side.

Fig. 5 (case 1).—Encephalogram showing internal hydrocephalus and cortical atrophy. Note the thin calvarium on the left.

There was no asymmetry of the extremities, and the neurologic examination gave normal results.

There was a congenital cardiac lesion, though the exact defect could not be determined.

The encephalographic findings were normal.

The films of the skull were suggestive of oxycephaly, although there was no distortion. The circumference of the head was 56.5 cm.

Comment.—In the majority of cases of hemihypertrophy as well as in cases of unilateral atrophy the condition has been described as congenital. The literature

on this subject is much less complete than that on atrophy of the opposite type, although some seventy cases of hemihypertrophy, including eight from the Mayo Clinic in 1933, have been reported. The most interesting and the only modern report with postmortem observations was made in 1916 by Hutchins,[5] who described the case of an infant, aged 5 months, with enlargement of all parts of the right side, including paired organs and glands, but with no asymmetry of the skull or brain. The findings in this case were ascribed by Turnball to hypertrophy of the right adrenal gland. In an earlier report Cagniati[6] described a case in which there was skeletal enlargement on the left. In this instance the skin was thickened; the blood vessels were hypertrophied, especially the media and the intima, and the supporting tissues of muscle, nerve fibers and peripheral ganglia were likewise hypertrophied. The nerves and the central nervous system were normal. Cagniati assumed the cause to be a disturbance in the mesenchyme in

Fig. 6 (case 2).—Photograph of the patient, showing reduced development of the left side of the face and thorax.

the first embryonic period. Cassirer[4] also referred to a case of von Ziehen,[4] in which details of pathologic changes in the central nervous system were not described but in which hypertrophy about the nerves of the eyelids and atrophy of the bulb were especially noted.

Case 3.—George R., aged 12½ years, one of ten children, was born after a difficult labor lasting twenty-four hours. The enlargement of the left side of the face and the tendency of the left eyeball to roll upward were noted immediately. Growth had always been retarded, and vision was defective; in addition, the boy was thought to have cardiac disease because of breathlessness on exertion.

5. Hutchins, Robert: Brit. J. Child. Dis. **13**:233, 1916.

6. Cagniati, quoted by Cassirer, R.: Die vasomotorisch- trophischen Neurosen, Berlin, S. Karger, 1912, p. 677.

At the age of 6 months he was very ill with scarlet fever. During his third year he had a single convulsion; after a second convulsion three years later, epilepsy became definitely established.

The essential observations were: The height was 50¾ inches (128 cm.) and the weight, 51 pounds (23.1 Gm.); the physical development was that of a boy between 9 and 10 years, and the intelligence quotient was 101. There was enlargement of the facial bones, jaw and orbit, but the skull was not involved. There was precocious dentition on the left.

Vision in the left eye was 10/200 and in the right eye 20/15. There was asymmetry of shape of the optic disks; the left was a long upright oval, and the right

Fig. 7 (case 2).—Roentgenogram, showing facial asymmetry.

was round. There was constant hyperphoria of 15 degrees on the left; amblyopia was thought to be due to disuse.

There was hypertrophy of both tonsils, that on the left being from three to four times larger than that on the right, filling the pharyngeal fossa and extending to the midline flush with the uvula.

A roentgenogram of the chest showed fulness of the pulmonic arch. Cardiac examination revealed systolic retraction at the apex; no murmurs were heard with the patient in the upright posture, but a to-and-fro murmur was audible with the patient in the recumbent posture and was regarded as a functional disturbance. Observations while the patient was in the ward showed a variation in the pulse rate, but tachycardia was the rule.

On removal, the tonsils exhibited the usual hyperplasia and infectious state, but a notable feature was the increase in the number and size of crypts and blood vessels of the left tonsil.

Fig. 8 (case 3).—Photograph of the patient showing hypertrophy of the left side of the face. Note the squint.

Fig. 9 (case 3).—Photograph showing enlargement of the upper teeth on the left side. Note the position of the first central incisor on the left in reference to the center of the oral cavity.

Comment.—In these cases it is interesting that anomalies of development were associated with general physical and glandular inferiority. In all cases the asymmetry is to be regarded as the result of trophoneurosis due to embryologic defects in the visceral centers of the nervous system.

DISCUSSION

DR. VICTOR E. GONDA: In the roentgenograms the sella turcica can be seen. In the first two patients the difficulty might have had something to do with disturbance of the pituitary gland.

DR. ARTHUR WEIL: Dr. Masten referred to the different theories to explain hemiatrophy of the body by assuming a defect in the formation of certain hypothetic vegetative centers in the brain or a lack of unilateral (?) endocrine stimuli. The fact that in such cases of hemiatrophy of the musculature and of the skeleton the condition may be combined with congenital malformation of other organs might speak in favor of the theory that hemiatrophy of the body is due more to some disturbances of development during fetal life than to postnatal defects. The following report of a case may illustrate such a combination: A woman, about 48 years old, presented the clinical picture of slowly progressing muscular atrophy involving chiefly the upper half of the right side of the body. At autopsy hemiatrophy of the left hemisphere of the brain was found, with pachygyria, agyria and islands of heterotopic gray masses within the corona radiata. The right hemisphere was normally developed. In the cervical region of the spinal cord there was demyelinization of the crossed fibers from the right side and, less marked, of the anterior corticospinal tract on the left. The right anterior horn was atrophic, the number of its ganglion cells was markedly reduced and the remaining cells showed more or less advanced fatty degeneration. The heterotopic islands of ganglion cells in the left hemisphere indicate a disturbance of development which must have occurred earlier than the fifth month of embryonic life. The contralateral degeneration of the right lower motor neuron with muscular atrophy, however, reached its maximum only during the fifth decade of life.

DR. ADRIEN VERBRUGGHEN: I had supposed that the idea that the right adrenal gland is responsible for hypertrophy of one side of the body had been satisfactorily disproved by this time. In Dr. Weil's case I wonder whether the patient could speak.

DR. R. M. STRONG: I wonder whether Dr. Masten has considered the possibility that in some cases the asymmetry is the result of a weak genetic composition. Similar or comparable cases were explained on this basis by Dr. Streeter of Baltimore before the Institute of Medicine here in Chicago a few years ago.

DR. MABEL G. MASTEN: The sella turcica in each of these cases was normal.

News and Comment

FORMAL OPENING OF HISTOLOGIC INSTITUTE IN MADRID

On Oct. 17, 1935, the first anniversary of the death of Ramón y Cajal, a new institute housing the Laboratorio de Histología Normal y Patológica, of which Dr. P. del Río-Hortega is the director, was formally opened in Madrid. Devoted entirely to research, this laboratory was founded in 1910 by Achúcarro and has been under the leadership of Dr. Río-Hortega since 1919. It is a part of the state educational system. From its previous quarters have been published fundamental contributions to the histology of the nervous system, such as the description of the pineal gland, of the microglia and of the oligodendroglia and, more recently, a series of monographs on the classification of tumors of the brain.

The new building is excellently designed and equipped. In addition to Dr. Río-Hortega's office and laboratory there are two histologic laboratories, each subdivided into spacious individual cubicles. Special rooms are devoted to zoological research and biologic chemistry. A separate suite is used for tissue culture, and there are in addition complete facilities for microdissection. In conjunction with the laboratories is an operating suite. The building also contains a lecture hall, a library and a room for collections. An entire floor is used as an animal farm. In the basement, apart from storerooms, are microtomes for cutting sections of the whole brain in pyroxylin (celloidin) and in frozen sections and a photographic laboratory which includes apparatus for cinemicrography.

The new institute, accommodating a total of twenty workers, is filled to capacity. The majority are Spaniards, but there are at present four foreign students. Dr. Río-Hortega plans to maintain approximately this ratio in future years.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION

The thirteenth annual meeting of the American Orthopsychiatric Association will be held at the Statler Hotel in Cleveland on Feb. 20, 21 and 22, 1936. Information may be obtained from Dr. George S. Stevenson, secretary, 50 West Fiftieth Street, New York.

INTERNSHIPS IN PSYCHIATRY

The Worcester State Hospital, Worcester, Mass., announces the establishment of six internships in psychiatry for periods of twelve months, starting July 1, 1936. The duties provide for a rotating service on medical, surgical and male and female psychiatric wards. Organized instruction will be given in the following: clinical psychiatry, administrative psychiatry, biopsychiatry, juvenile psychiatry, psychiatric social service, neuropathology, fever therapy, the endocrine glands in psychiatry, research methodology, psychometrics in psychiatry and biometrics. Registration must be made before March 1, and an examination will be held on March 15 at 9 a. m. at the hospital. The hospital provides maintenance. Graduates (unmarried men) of class A medical schools who have completed an accredited internship in medicine are eligible. Applications should be addressed to the Director of Clinical Psychiatry.

Obituary

JOHN LEONARD ECKEL
1880–1935

A familiar figure in the neurologic world is today deeply mourned. Dr. John Leonard Eckel died in service on Nov. 27, 1935. While ill with grip, he left his bed to attend his patients and at the bedside of one of them succumbed to a heart attack. This is the dramatic exit of a man who from a humble beginning arose to international recognition in his particular field.

Dr. Eckel was born in Perrysburg, Ohio, on April 28, 1880. He received his premedical training at the University of Michigan and the degree of Doctor of Medicine from the University of Buffalo School of Medicine in 1907. His efforts to obtain a medical education were beset with many difficulties.

He served his internship at the East Manhattan State Hospital of New York and was junior assistant physician at the same hospital. In 1909 he was junior assistant physician at the Buffalo State Hospital, and the following year, senior assistant physician.

In 1911 Dr. Eckel entered the University of Berlin, doing special work in nervous and mental diseases. He attended the University of Munich for one semester, working in the neuropathologic laboratory under Professor Alzheimer and doing clinical work in the wards and the psychiatric hospital in charge of Professor Kraepelin. He also spent one semester at the University of London, National Hospital for the Paralyzed and Epileptic, Queen Square.

On Jan. 1, 1913, Dr. Eckel returned to Buffalo and began private practice. He was appointed to the faculty of the University of Buffalo School of Medicine, where he occupied the chairs of associate professor of neurology and assistant professor of psychiatry, positions which he held to the day of his death.

Always actively interested in scientific research, Dr. Eckel again returned to the University of Vienna to study for three and one-half months. In January 1926, as evidence of his intensive research, he published an article entitled "Encephalitis Acutissima." Most of his research work was done in Philadelphia, where he went from Buffalo once a month for over fifteen years.

Dr. Eckel was attending and consulting neurologist and psychiatrist in the following hospitals in Buffalo: the Buffalo General Hospital, the Millard Fillmore Hospital, the Memorial Hospital, the Mercy Hospital, Our Lady of Victory Hospital, the Sisters' Hospital, the Providence

Retreat, the Crippled Children's Guild, the Buffalo City Hospital, the Emergency Hospital and the J. N. Adam Memorial Hospital at Perrysburg, N. Y.

He always kept in close touch with colleagues in his profession, being a member of the Buffalo Academy of Medicine, the Erie County Medical Society, the New York State Medical Society, the American Medical Association, the American Psychiatric Association, the American Neurological Association, the American Association for Research in

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Nervous and Mental Diseases, the New York Neurological Society, the Philadelphia Neurological Society, the Central Neuropsychiatric Association and the American Association for the Advancement of Science. He has held offices in the following societies: secretary of the Section of Pathology and Bacteriology of the Buffalo Academy of Medicine in 1914-1915 and chairman of this section in 1915-1916; vice chairman of the Section on Nervous and Mental Diseases of the American Medical Association in 1927-1928 and chairman of this section in 1928-1929;

president of the Central Neuropsychiatric Association in 1930-1931; vice chairman of the Section on Nervous and Mental Diseases of the New York State Medical Association in 1933-1934 and chairman of this section in 1934-1935, and president of the Buffalo Neuro-Psychiatric Society from 1932 to 1935.

Dr. Eckel read papers at the joint meeting of the British and American Neurological Societies in London on July 28, 1927; the First International Congress on Neurology in Bern, Switzerland, on Sept. 3, 1931; the Pan-American Medical Congress in Dallas, Texas, in May 1933; the Pan-American Medical Floating Congress in March 1934; the Second International Congress on Neurology in London on Aug. 1, 1935, and at meetings of the many neurologic and psychiatric associations and medical societies of which he was a member.

During the World War, Dr. Eckel served as secretary to the local medical advisory board and held the commission of captain in the United States Army.

In a life so fully occupied, Dr. Eckel also found time for social and fraternal activities. He was a member of the Saturn Club, the University Club, the Buffalo County Club, the Torch Club, the Scholia, the Library Association, the Institute of American Genealogy, the Archaeological Institute of America, the University of Buffalo Alumni Association and the Phi Chi medical fraternity. As a good citizen he was keenly interested in the proper development of his community and was thoroughly practical in the aid he gave to humanitarian and welfare projects.

In 1914 he married Berenice Long, an accomplished violinist. There were no children.

Dr. Eckel has left the neurologic field much enriched by his tireless efforts and fruitful contributions. He was highly esteemed by his colleagues for his profound knowledge in his chosen profession, and by those who were privileged to know him well he was loved for his humaneness, tolerance and sterling character.

N. W. WINKELMAN.

Abstracts from Current Literature

Anatomy and Embryology

LARYNGEAL NERVES. EDWARD F. ZIEGELMAN, Arch. Otolaryng. **18**:973 (Dec. 19) 1933.

In a well illustrated article, presenting the results of numerous dissections, the author states that the recurrent nerve, being a branch of the vagus nerve, may be affected in conjunction with the main nerve as a result of a lesion that is either supranuclear or in the main trunk. In addition, it may be involved at any place along its tract, that is, from the parent stem, the vagus, to its ultimate distribution in the larynx. Most of these lesions are due to trauma of some kind incurred during surgical procedures on the thyroid gland. Of the forty-two dissections of recurrent laryngeal nerves, twenty-three were on the right side and nineteen on the left. As a general rule, the nerve on the left side was somewhat deeper in the neck than that on the right. It occupied more closely the usual site described in textbooks, the tracheo-esophageal groove. In nine of the twenty-three dissections on the right side the nerve lay anterior to the inferior thyroid artery. In eight instances the nerve was between the two main divisions of the artery. In six instances the nerve was definitely posterior to the artery. On the left side a somewhat similar condition was observed. Six dissections showed the nerve anterior to the artery; in seven instances it was between the main branches, and in six it was posterior to the artery.

The relation of the nerve to the capsule of the gland was observed to be different from that described in most textbooks. The capsule is usually mentioned as being formed by splitting of the second layer of the cervical fascia. Thus the gland is supposed to be surrounded completely by the capsule, and the nerve is accepted as assuming a position at all times posterior to it. This supposed fact was one of the reasons for the development of the intracapsular technic of lobectomy. Moreover, the modern method of ligation of the artery at the capsule was accepted as being devoid of the least danger to the nerve. Observations do not bear this out. This fascial capsule continues for a distance equal to approximately two thirds of the posterior surface of the gland. It is then reflected on the esophagus. A thin modified sheath is continued over the remaining portion of the posterior mesial surface of the respective lobes. The nerve on each side, in practically all of the dissections, was observed to leave this true capsule and occupy a position in close contact with the gland on its inner posterior mesial surface. This makes this portion of the gland the dangerous area in thyroidectomy. The course of the external branch of the superior laryngeal nerve impresses one with the ease with which it may be injured or severed in ligation of the superior artery in continuity. This is particularly true if transfixion is used. It seems that the safest method, so far as limiting the danger to the external branch of the superior laryngeal nerve is concerned, is to ligate the vessel as near the upper pole and the capsule as possible. The recurrent nerve was demonstrated as entering the larynx beneath the inferior constrictor muscle, posterior to the inferior cornu of the thyroid cartilage. The internal branch of the superior laryngeal nerve after entering the thyrohyoid membrane was easily demonstrated beneath a fold of mucous membrane in the sinus pyriformis.

The following conclusions were made: The recurrent laryngeal nerve may assume a variable position. This is particularly true in its relation to the inferior thyroid artery. This fact impresses one with the wisdom of ligating the artery at some distance from the gland. The nerve apparently leaves the true capsule to assume a position in close relation to the posterior mesial third of the gland proper. This is the dangerous area for injury to the nerve. In all of my dissections the

nerve entered the larynx posterior to the inferior cornu, which indicates that this structure is a definite surgical landmark for protection to the nerve. This external branch of the superior laryngeal nerve is in close relation with the superior thyroid artery; it can be injured in ligation of this vessel unless caution is used. The internal branch of the superior laryngeal nerve sends branches which communicate with the recurrent nerve. In most cases it supplies the interarytenoid muscle; this is contrary to the usual teaching.

R. J. HUNTER, Philadelphia.

EXPERIMENTAL STUDIES ON THE INTRINSIC FIBERS OF THE CEREBELLUM. JAN JANSEN, J. Comp. Neurol. **57**:369 (June) 1933.

The existence of short arcuate fibers connecting neighboring folia of the cerebellar cortex is well established. Jansen is here interested in the existence of intralobular and interlobular association fibers. Small and superficial lesions were produced in the brains of thirty-six rabbits. After from two to three weeks the brains were prepared by the Marchi method. The investigation was based on ten series of sections. The lesions were in (1) the flocculus and the lobulus petrosus, (2) the vermis and (3) the hemispheres. Jansen confirms the observation that circumscribed cortical lesions in any part of the cerebellum cause degeneration in the folia adjacent to the lesion. Degeneration in more remote regions is also found. When the flocculus was injured all folia of the lobulus petrosus showed degenerated fibers. Injuries to the cortex of the hemisphere were followed by degeneration not only in the vicinity of the lesion but also in the vermis and to a lesser extent in the contralateral hemisphere. When the vermis was injured the folia immediately in front of as well as behind the edge of the lesion showed degenerated fibers. Jansen concludes that no association tracts go from the vermis either to the hemispheres or to the lobulus petrosus but that there are association fibers which go from the cortex of the hemisphere to the vermis. The hemispheres are interconnected by association fibers which, partly at least, seem to have the character of a commissure. The author's observations confirm the impression of the mutual independence of the main cerebellar lobes, as maintained by Clarke and Horsley.

ADDISON, Philadelphia.

THE VESTIBULAR CLUB ENDINGS IN AMEIURUS: FURTHER EVIDENCE ON THE MORPHOLOGY OF THE SYNAPSE. G. W. BARTELMEZ and N. L. HOERR, J. Comp. Neurol. **57**:401 (June) 1933.

This study deals with club-shaped endings of certain root fibers of the eighth nerve on the lateral dendrite of Mauthner's cell in the teleost catfish. The brains were fixed by perfusion with rapidly penetrating, good cytoplasm-fixing fluids and stained by the newer cytologic methods, such as those of Bensley and Kull. This gave more reliable pictures than did the silver impregnation methods which were also used.

Bartelmez had previously pointed out that the club-shaped endings of primary neurons from the sacculus on the lateral dendrite of Mauthner's cell offer a favorable synapse for study because of the large size of the cell. Mauthner's cell is one of a group of large elements which lies at the transverse level of the eighth root and dorsal to the rest of the motor tegmental nucleus. In Ameiurus larvae of 10 mm., both the root fibers and the axon of Mauthner's cell are myelinated. At this stage of development Mauthner's fiber gives off collaterals to all levels of the somatic motor column caudal to its cell body, so that there is a direct pathway for impulses from the sacculus to the musculature employed in swimming. Neurofibrils run in the long axis of both the dendrite and the club. The mitochondria of the clubs are rod-shaped. Bartelmez and Hoerr present evidence that each of the elements of the synapse has a limiting membrane and state that there is never any continuity between the club and the dendrite. They believe from a cytologic point of view that all reduced silver methods are reliable only so far as they can be checked by other methods.

FRASER, Philadelphia.

ON THE AREA OF THE SUNKEN CEREBRAL CORTEX AS DETERMINED FROM THE LENGTH AND DEPTH OF SELECTED SULCI IN THREE CLASSES OF HUMAN BRAINS: SCHOLARS, HOSPITAL WHITES, HOSPITAL NEGROES. W. H. F. ADDISON and H. H. DONALDSON, J. Comp. Neurol. **57**:429 (June) 1933.

The purpose of this study was to determine how the proportional areas of the different lobes were related in the brains of scholars and those of hospitalized white persons and Negroes. The material available consisted of the brains of three male scholars, thirty hospitalized white men and twenty-seven hospitalized Negro men. Twenty sulci were measured for lengths and depths according to the method used by Canavan in the study of the brains of E. E. Southard and his parents. By a series of tables Addison and Donaldson present evidence from which they conclude that there is a high degree of constancy in the relative extent of the cortical areas of the four lobes of the human brain; that comparison according to mental status (hospitalized white persons and scholars) indicates a somewhat greater temporal area in the scholars' brains, and that the outstanding characteristic of the scholars' brains is the lesser depth of their sulci. The authors interpret this last characteristic as due to the better development of the associational system of fibers; it is considered as one anatomic factor contributing to the higher mental status of the group of scholars. FRASER, Philadelphia.

THE STATUS OF METAMERISM IN THE CENTRAL NERVOUS SYSTEM OF CHICK EMBRYOS. G. L. STREETER, J. Comp. Neurol. **57**:455 (June) 1933.

The purpose of this study was to verify the presence or absence of transitory metameric segmentation of the central nervous system. Since neural segmentation is frequently portrayed in the chick, Streeter has restudied the embryo of this form with modern appliances for dissection and photography. At the four-somite stage earlier observers have figured eleven segments in the brain tube, but the author does not find this segmented condition. The nearest approach to metameric segmentation in the brain is in that portion of the neural tube from which the visceral cranial nerves arise. This region shows a series of transverse grooves, corresponding to the regions of the nerves. In the spinal region there is even more definite segmentation, but this is not primarily in the neural tube but secondary to the segmental division of the mesoderm into somites. Instead of being a rigid metameric system, the neural tube shows itself responsive at all levels to its environment. Streeter comments on the subdivision of the embryonic brain into three primary vesicles and objects to the acceptance of the three subdivisions as serially equivalent, instead of regarding them as the result of differentiations going on within their constituent neurons in adaptation to many internal and external forces. ADDISON, Philadelphia.

THE DEVELOPMENT OF LATERAL-LINE SENSE ORGANS IN AMPHIBIANS OBSERVED IN LIVING AND VITAL-STAINED PREPARATIONS. L. S. STONE, J. Comp. Neurol. **57**:507 (June) 1933.

This is one of a series of studies on the lateral line organs by Stone. In this study, using mostly embryos and larvae of Amblystoma punctatum, the author employed a combination of technics and has been able for the first time to observe a sense organ in the living animal throughout its entire development. Ectoderm containing a postauditory placode in a normally pigmented amblystoma of the tail bud stage was excised and exchanged for a similar transplant from an embryo of the same stage stained with nile blue sulfate. The blue lateral line primordium is seen to move caudad, segmenting into beadlike groups which are deposited in its pathway as clumps of blue cells radially arranged. These form both the sensory and the supporting cells of the lateral line sense organs without any contribution from the surrounding ectodermal cells of the host. The development of accessory organs is by budding of supporting cells at definite poles of the primordial organ.

The pole of an organ most readily brought into the budding stage is the one directed toward a rapidly proliferating region. The essential features of development are the same in both urodeles and anurans.

ADDISON, Philadelphia.

A CONTRIBUTION TO THE CEREBRAL REPRESENTATION OF THE RETINA. STEPHEN POLJAK, J. Comp. Neurol. **57**:541 (June) 1933.

The terminations of the retinal quadrants on the primary visual centers are well established in experimental animals. The purpose of this study was to extend the investigation to the central portion of the visual pathway, from the lateral geniculate body to the occipital cortex. Monkeys were used for the experiments. Lesions were made in the occipital lobe. The lobe and the lateral geniculate body were sectioned serially and stained by the Nissl method. The optic radiations were treated by the Marchi method, and these results have been previously reported. By varying the size and location of the lesion Poljak proved that the upper homonymous quadrants of both retinas, excluding the macula, are represented in the upper dorsal horizontal branch of the visual radiation and in the upper lip of the calcarine fissure; the lower quadrants, in the lower horizontal branch of the radiation and in the lower lip of the same fissure, and the macula, in the axial branch of the radiation (placed in its center) and in the occipital operculum. The entire retina is represented exclusively and entirely in the striate area of the occipital lobe. Another series of experiments was done to demonstrate whether the portion of the external geniculate body on which the macula is projected has a bilateral representation. In this series the striate area on one side was partially or totally removed. In such animals no degeneration of the contralateral lateral geniculate body was seen after complete extirpation of the striate area. No decussating fibers were seen.

In still other experiments smaller and larger lesions were made in the occipital region, and zones of degenerated cells were found in the ipsilateral lateral geniculate body. These were in fair agreement with the number, position and size of the lesions of the visual radiation and of the cortex, which makes it plausible that each small segment in the visual radiation has its own small projection area in the striate cortex. When lesions of the striate area were made in a pattern, a fairly accurate figure of the zones of degeneration was produced in the ipsilateral lateral geniculate body.

These careful studies on the monkey show a point-to-point representation of the external geniculate body on the ipsilateral striate area. If the retina has a point-to-point representation on the external geniculate body, the retina would likewise have a point-to-point representation on the occipital cortex.

FRASER, Philadelphia.

THE EPIBRANCHIAL PLACODE OF THE FACIAL NERVE IN AMBLYSTOMA JEFFERSONIANUM. F. L. LANDACRE, J. Comp. Neurol. **58**:289 (Aug.) 1933.

This article is one of a series on the epibranchial placode of the facial nerve. Using a close series of Amblystoma embryos, stages from 24 to 50 inclusive, Landacre describes the history of the epibranchial placode from the time it begins to thicken in the nervous layer of the ectoderm. In this position it goes through a growth period, and after this it becomes detached from the ectoderm, migrates inward to join the remainder of the facialis ganglion derived from the neural crest and from the dorsolateral placode. The author thus believes that the epibranchial placode is wholly ectodermal in origin and that the facial ganglion of Amblystoma has a triple origin.

ADDISON, Philadelphia.

THE BASAL DIENCEPHALON OF THE ARMADILLO. HOWARD A. HOWE, J. Comp. Neurol. **58**:311 (Oct.) 1933.

Five sets of serial sections of the brain of the nine-banded armadillo were available for this study. These were cut in three planes and for the most part

were stained by the Pal-Weigert and Nissl methods. The coronal sections were found most useful because the relations of the region are primarily longitudinal. Grossly, the brain of the armadillo resembles that of the rodent. The subthalamus comprises the nucleus reticularis, zona incerta, corpus Luysi and field of Forel. Its cells appear to be morphologically motor. It is connected with the midbrain and the medulla through the posterior (median) longitudinal fasciculus. The hypothalamus comprises about twelve nuclei, differentiated mainly on the basis of topography, definite concentration of similar elements and isolation of areas by unmistakable cell-free zones. This nuclear configuration was found to parallel closely that described for the rats and carnivores used in the laboratory.

FRASER, Philadelphia.

THE ANATOMY OF THE BRAIN OF THE WHALE (BALAENOPTERA SULFUREA). RICHARD B. WILSON, J. Comp. Neurol. **58**:419 (Oct.) 1933.

The present investigation on the brain of the whale is concerned with the general morphology of the entire brain and with the more detailed anatomy of the medulla oblongata. As seen from above, the contour of the whole brain is approximately that of an egg. Its total weight without membranes is 5,678 Gm. The cerebellum weighs 18.95 per cent of the total weight of the brain. The frontal and temporal lobes are poorly developed, and thus the insula lies exposed. There is no olfactory tract in the animal. The neopallial fissures of Balaenoptera sulfurea in general arrangement resemble those of other Cetacea, with the exception of the arcuate fissures, which resemble more closely those in Carnivora. The commissures, except the commissura mollis, are readily recognized. The corpus striatum is strikingly small compared with the thalamus.

ADDISON, Philadelphia.

THE VASCULARITY OF PARTS OF THE CEREBELLUM, BRAIN STEM, AND SPINAL CORD OF INBRED ALBINO RATS. E. HORNE CRAIGIE, J. Comp. Neurol. **58**:507 (Oct.) 1933.

The method used in this work is one frequently employed by the author—that of injecting carmine gelatin into the blood vessels of the brain and measuring the length and diameter of capillaries in certain areas. The animals used were albino rats produced from mating of litter brothers and sisters for from sixty-three to sixty-five generations by Dr. Helen Dean King of the Wistar Institute. The results obtained are compared with the findings in ordinary albino rats and in wild Norway rats. The diameters of the capillaries in the selected eight regions show no significant differences among each other from those in ordinary albino rats. However, the diameters are consistently, and in most cases significantly, lower than in the wild Norway rat. The measurements of the total length of capillaries in a unit volume of tissue correspond with those in groups of rats previously studied. The divergence from the findings in ordinary albino rats corresponds in all cases with the observations in wild Norway rats. Thus close agreement between the inbred albino rats and the wild Norway rats as previously found in the archicortex is here confirmed in the cerebellum, brain stem and spinal cord.

FRASER, Philadelphia.

A HISTOLOGICAL STUDY OF THE TISSUES OF ANIMALS SURVIVING COMPLETE EXCLUSION OF THE THORACICO-LUMBAR AUTONOMIC IMPULSES. SAM L. CLARK, J. Comp. Neurol. **58**:553 (Dec.) 1933.

Tissues from a female cat which had survived complete sympathectomy for a number of years were available and also material from a male dog and a male cat in which the cervical sympathetic chains and the semilunar ganglia were left in place but not connected with the central nervous system. The dog had lived almost two years and the cat for over three years. All three had been used in experiments in the laboratory of Dr. W. B. Cannon. The animals were killed by

bleeding, and the tissues were rapidly removed to fixative. Histologic changes in the non-neural tissue were not striking. The smooth muscle existed and performed its activities. The mammary glands showed pigment in section. The reproductive organs in the case of the male cat and the dog showed a change in the testes. Mature sperm cells were found in only 40 per cent of the sections of the tubules of the dog and in 10 per cent of the tubules of the cat. The thyroid glands of the cats showed two chief peculiarities which did not occur in the gland of the dog: 1. There was a great difference in size of the follicles of both glands, which varied from very small to large, irregular ones. 2. Numerous granules of brownish-yellow pigment were present in the cells of the follicles. The alterations in the thyroid glands of the two cats, the pigmentation of the mammary gland cells of the female cat and the reduction in the number of spermatozoa in the testes of the two male animals seem to be indirect results of the general absence of sympathetic impulses rather than the direct effect of denervation of the specific organs.

Histologic pictures in the nervous tissue were interesting because the visceral efferent neurons existed without their usual postganglionic connections, and the postganglionic neurons existed without preganglionic connections. Pericellular skeins were more abundant in the dorsal root ganglia of sympathectomized animals than in the dorsal root ganglia of normal controls. It seems that the removal of the sympathetic system produced less conspicuous changes than might be expected from such an operation.

ADDISON, Philadelphia.

THE POSTERIOR CALCARINE FISSURE IN THE DOG. HAROLD A. COHN and JAMES W. PAPEZ, J. Comp. Neurol. **58**:593 (Dec.) 1933.

Cohn and Papez have attempted to estimate the frequency in the brains of dogs of a sulcus resembling the calcarine sulcus of primates and the extent of, and relations of the visual area to, that sulcus. The two occipital poles were examined in 100 brains. Sixty-four per cent showed a well developed posterior calcarine fissure in both hemispheres. In 15 per cent of the cases it was totally absent in both hemispheres. For a certain number of dogs a record was kept of their breed, age, sex and size, but no correlation could be observed between these factors and the incidence of the development of the fissure. For the histologic study a primary mordanting in potassium bichromate brought out the line of Gennari, which was used as a guide to the localization of the visual cortex. The visual area was seen surrounding the posterior calcarine fissure as far as the occipital pole. The posterior calcarine fissure is thus seen to be one of common occurrence in the brains of dogs and is analogous to the fissure observed in primates both as to position and as to histologic structure.

ADDISON, Philadelphia.

NEUROFIBRILLAR DEVELOPMENT IN THE CENTRAL NERVOUS SYSTEM OF CAT EMBRYOS BETWEEN 8 AND 12 MM. LONG. WILLIAM F. WINDLE, J. Comp. Neurol. **58**:643 (Dec.) 1933.

This is one of a series of studies on the embryonic development of nerve cell groups and fiber pathways. For this paper twelve embryos of known ages (from 20 to 22 days) were treated with pyridine silver and cut in three planes. At least four important fiber groups besides the fasciculus longitudinalis medialis undergo development in the forebrain from the twentieth to the twenty-second day. These have been designated olfactory, striothalamic, thalamostrial and juxta-optic pathways, although it is not known what tracts they form in the adult. The fasciculus longitudinalis medialis arises from a prominent but poorly circumscribed group of neuroblasts, apparently entirely from the same side, and descends through the midbrain ventral to the motor neuroblast column.

All motor nerves arise from a single longitudinal column of neuroblasts placed in the medial part of the basal plate. The visceral cell groups arise medial to the somatic cell groups in this column, but migrate laterad. Some of the somatic

motor nuclei shift their positions longitudinally, although this process seems to be entirely passive.

All afferent nerves are present in the embryos of this series, but even in the 11.5 mm. embryos the olfactory nerve contains no neurofibrils and the optic and cochlear nerves are less mature than the others. The semilunar ganglion is very prominent. As the fibers of the sensory root of the trigeminal nerve enter the rhombencephalon, the ones from each portion of the semilunar ganglion maintain their identity to some extent. Those from the ophthalmic portion enter the most ventromedial part of the tract; those from the mandibular portion pass farthest lateral and dorsad, and the maxillary ones occupy a position that is intermediate. Primary sensory pathways are: (1) the spinal tract of the trigeminal and vestibular nerves, which contains some bifurcating fibers of the facial, glossopharyngeal and vagus nerves; (2) the posterior spinal funiculus, containing fibers from the hypoglossal nerve; (3) the tractus solitarius; (4) the mesencephalic tract of the trigeminal, and (5) a unisegmental vestibular bundle.

An extensive system of association and commissural neuroblasts develops in the lateral wall of the neural tube. Their axons form longitudinal pathways. The determination of the neurofibrillar development in cat fetuses makes it possible for Windle to correlate anatomic observations with the development of fetal behavior.

ADDISON, Philadelphia.

A DETERMINATION OF THE NUMBER OF NERVE FIBERS IN THE EIGHTH THORACIC AND THE LARGEST LUMBAR VENTRAL ROOTS OF THE ALBINO RAT. DONALD DUNCAN, J. Comp. Neurol. **59**:47 (Feb.) 1934.

Agduhr has observed in the house rat and in the mouse an increase in the number of fibers in the ventral root with the increase in age and also an increase in the number of nerve cells. Donaldson and his school have presented data to show that the maximum number of nerve elements in the albino rat is fixed within the first twenty days after birth. Duncan has entered the controversy, using Agduhr's method on albino rats. The eighth thoracic and the largest lumbar nerves (fifth or sometimes fourth) were selected for study. The latter is essentially a pure somatic nerve and the former is a somatic and visceral efferent nerve. The nerve, ganglion and roots were removed in a single piece and treated with Ranson's pyridine technic to stain the axis-cylinders. Similar pieces from the opposite side were treated with 1 per cent osmic acid to show the myelin sheath. The average numbers of fibers in the largest lumbar root of males are 1,913 for rats from 18 to 50 days old, 1,940 for adult rats from 136 to 300 days old and 799 for senile rats from 548 to 800 days old. The average figures for the ventral root fibers of the eighth thoracic nerve are 1,122 for young rats, 1,268 for adults and 1,128 for senile animals. The number of fibers in female rats is less by from 10 to 20 per cent than in males, but this difference is about equal to the difference in body size. Duncan concludes that the number of ventral root fibers in the albino rat does not increase after the twentieth day and that the degenerating fibers, seen in normal animals and which he has previously reported, are not replaced but are permanently lost. He believes that an improved method of staining would not reveal a significantly greater number of fibers than is reported here.

FRASER, Philadelphia.

ARE THERE EFFERENT FIBERS IN THE DORSAL ROOTS? J. C. HINSEY, J. Comp. Neurol. **59**:115 (Feb.) 1934.

For this study, the lumbosacral roots of adult cats were exposed. Selected dorsal roots were isolated, tied and sectioned distal to the ligature. Time was allowed for peripheral degeneration, and then the animals were killed. The proximal stumps were treated by the pyridine silver technic, and the dorsal root ganglia of these nerves, together with the ventral root and a portion of the peripheral nerve, were treated by the Marchi technic. In the proximal stump after sixteen days there were no persisting fibers. In the distal stump there was no degeneration, except that

which could be attributed to trauma. In another series the dorsal root ganglia were removed completely. After varying intervals the animals were killed. The spinal segments with the appended roots were prepared by the pyridine silver staining. Serial sections of the spinal cord segments were made transversely, horizontally and sagittally. Preparations stained with pyridine silver and cut in different planes did not support the presence of efferent fibers in the dorsal roots.

ADDISON, Philadelphia.

CELLS AND FIBERS IN SPINAL NERVES: II. A STUDY OF C2, C6, T4, T9, L3, S2 AND S5 IN MAN. H. A. DAVENPORT and R. T. BOTHE, J. Comp. Neurol. **59**:167 (Feb.) 1934.

Seven spinal nerves, with the roots, ganglia and nerve as far as the dorsal ramus, were fixed in a solution containing 4 per cent formaldehyde and 5 per cent glacial acetic acid. Each specimen was divided into three parts. The proximal portion and the distal portion were put into osmic acid. The middle portion, containing the dorsal root ganglion together with short lengths of cell-free nerve on each end, was embedded without staining and treated by the silver technic of Davenport and Ranson. Cells and fibers were then enumerated in representative areas and estimated for entire areas. The results lead the authors to suggest the following generalizations: 1. The number of nerve fibers in the dorsal root is equal to the number of nerve cells in the ganglion. 2. The sum of the fibers in the dorsal and ventral roots is equal to the number found in the complete spinal nerve just distal to the ganglion. 3. There are more fibers demonstrable by silver stains in the dorsal roots and in most of the ventral roots than there are sheaths blackened by osmic acid. 4. More myelinated fibers are found distal than proximal to the ganglion.

FRASER, Philadelphia.

THE RELATION OF TASTE BUDS TO THEIR NERVE FIBERS. T. W. TORREY, J. Comp. Neurol. **59**:203 (April) 1934.

Ameiurus nebulosus, the common catfish, was used in this study. The catfish has taste buds on its barbels, and these taste buds are supplied by nerves coming from the geniculate ganglion of the seventh nerve. Each barbel is supplied with a large central nerve trunk which runs throughout its length. This gives off large branches which divide and redivide, so that all the buds at a particular level of a barbel are supplied by fibers which originate in the central trunk at a point far posterior to that level. Degeneration of myelin was seen as early as twenty-eight hours after the nerve was cut. This degeneration increased until at the end of ten days it was at its characteristic height. Taste buds did not disappear until secondary degeneration was greatly advanced, that is, from ten to thirteen days after cutting the nerve, depending on the temperature. The order of degeneration of the taste bud in a barbel was centrifugal. Electrical stimulation of the peripheral stump of a nerve severed at the base of a barbel induced the taste buds to disappear in advance of those of an unstimulated control. Low temperatures inhibited degeneration of the taste bud. The influence of heat and electrical stimulation is believed by Torrey to be directed against a physiologic or nutritional prerequisite of the normal taste buds. This prerequisite assumes the form of a hormone-like material present in nerves and is conceived of as being identical with that necessary for the maintenance of the nerve itself.

FRASER, Philadelphia.

FURTHER EXPERIMENTAL STUDIES ON THE INNERVATION OF STRIATED MUSCLE. HERBERT J. WILKINSON, J. Comp. Neurol. **59**:221 (April) 1934.

In a second study on the innervation of striated muscle Wilkinson describes experiments in which the sympathetic nerves in the intercostal, interosseal and lumbrical muscles of the cat were isolated by section of the somatic nerves. The

thoracic nerves from the fifth to the ninth, inclusive, were cut as far distally as possible without damage to the sympathetic ganglia or their rami communicantes. Fourteen days were allowed for degeneration of the nerves. The muscles were then stained according to the Bielschowsky technic, and the sections were studied serially. The sympathetic nerves were found only in relation to the blood vessels, and no evidence was found to support the hypothesis that striated muscle fibers are innervated by both the somatic and the sympathetic nerves. No evidence was found in favor of the existence of a neurofibrillar periterminal network which could be regarded as a transition between the neurofibrils of the motor axon and the substance of the muscle fiber.

ADDISON, Philadelphia.

THE EFFECT OF STIMULATION UPON THE COELIAC GANGLION CELLS OF THE ALBINO RAT. EVERETT H. INGERSOLL, J. Comp. Neurol. **59**:267 (April) 1934.

This investigation was undertaken to determine the effect of stimulation on autonomic ganglion cells and the sequence of changes in these cells during excitation and following its cessation. Under light ether anesthesia, the viscera were manipulated by gentle handling for a period of five minutes, followed by a minute of complete undisturbed rest and then exposure to air for one and one-half minutes; then the entire procedure was repeated. The celiac ganglia were removed rapidly after death and fixed in formaldehyde and mercuric chloride. Seven hundred and seventy-two cells and their nuclei were drawn and measured. Following the procedure of Bradshaw, the cells of the autonomic ganglia of the albino rat were classified into nine types according to the quantity and distribution of the chromidial substance. These nine types were grouped into three classes. The first class represents the resting and hyperchromatic phases of functional activity and has an average of over 50 per cent. The second class is distinguished by the aggregation of the chromidial substance around the nucleus and averages about 30 per cent. The third class is that of lightly staining cells. These cells represent the remaining 20 per cent. Stimulation of the abdominal viscera produced changes in the ganglion cells, as evidenced by the shifting percentages in the types of cells. This shift is definitely correlated with the length of period of stimulation. Class 1 decreases in number, while class 3 increases and class 2 remains fairly constant. The sizes of the cells and of their nuclei decrease as stimulation is prolonged. The sizes of the cells vary to a greater extent than do the sizes of the nuclei.

ADDISON, Philadelphia.

THE MOTOR NERVES OF THE EYE IN ALBINO AND GRAY NORWAY RATS. EDWARD MCCRADY JR., J. Comp. Neurol. **59**:285 (April) 1934.

The eyeballs of albino rats are heavier by some 15.7 per cent than those of the gray rat. On the other hand in the albino rats the optic nerves are about 12 per cent smaller, and the visual cortex is less well developed and thinner. The purpose of the study reported in this paper was to examine the motor nerves to the voluntary muscles of the eye in these two forms. Animals about 200 Gm. in weight were used. The tissue containing the gasserian ganglion, the internal carotid artery and the third, fourth and sixth nerves, together with the surrounding dura mater, was placed in 1 per cent solution of osmic acid. Sections were studied from each side of five animals of each sex of each race. The ten largest fibers of the third, fourth and sixth nerves in each animal were measured and averaged. The lateral rectus muscle was removed and weighed while fresh. McCrady found that the albino rats have more fibers in the motor nerves of the eye and larger external rectus muscles but that the gray rats have larger individual nerves fibers. The number of fibers in the motor nerves of the eye seems to be correlated with the size of the muscle supplied and the weight of the eyeball. The size of the fibers in the motor nerves of the eye seems to be correlated with the complexity of the central connections and of the sensory capacity of the eye.

ADDISON, Philadelphia.

THE FREQUENCY OF ATYPICAL NEURONS IN THE SPINAL GANGLIA UNDER NORMAL CONDITIONS AND AFTER LESIONS OF THE ROOTS, NERVES OR GANGLIA. R. W. BARRIS, J. Comp. Neurol. **59**:325 (April) 1934.

In the cat's spinal ganglia, in addition to the simple unipolar type of cell, there are atypical cells with end-bulbs which represent the terminal expansions of processes arising either from the cell body or from the axon and atypical cells with pericellular or periglomerular plexuses. In ganglia, the largest of which contain about 31,000 cells, the atypical cells ranged from 13 to 59. Experiments were performed to see if section of the sensory fibers in the peripheral nerve or dorsal roots at considerable distances from a ganglion caused an increase in the number of atypical cells in the ganglion. In four cats the left sciatic nerve was cut in the upper part of the thigh. In other cats the dorsal roots of certain lumbar and sacral nerves were cut close to the spinal cord. In still other cats the seventh lumbar and first sacral ganglia were incised with a scalpel. Varying periods of time were allowed for degeneration. Section of the sensory fibers in the peripheral nerve or dorsal roots at considerable distances from the ganglion did not cause an increase in the number of atypical cells, but direct incision of the ganglion produced a noticeable increase in the number of pericellular and periglomerular plexuses.

FRASER, Philadelphia.

ON THE CUTANEOUS NERVE AREAS OF THE FOREARM AND HAND—THEIR SIZES, VARIATIONS AND CORRELATIONS STUDIED IN A SMALL SAMPLE OF YOUNG ADULT MALES. J. MACLAREN THOMPSON, VERNE T. INMAN and BERNARD BROWNFIELD, Univ. California Pub. Anat. **1**:195, 1934.

The major objective of this study was to obtain a method of defining and measuring all the cutaneous nerve areas with their overlaps in a definite region of the body in a single subject. This paper deals with the cutaneous nerve areas of the forearm and hand: the medial, lateral and dorsal cutaneous nerves of the forearm, the ulnar and median nerves and the superficial branch of the radial nerve.

The method of outlining these cutaneous nerve areas for light touch is similar to that already published by Thompson and Inman (1933). The method is based on the fact that when a nerve is stimulated by a suitable current from an Alexanderson alternator, the cutaneous area supplied becomes so insensible to tactile stimuli that it can be outlined. This type of insensibility is termed "masking" (Thompson, 1933). The success of this technic depends on close cooperation between observer and subject. The subject is responsible for identifying the truly optimum position of the electrode: that which elicited the maximum area of tingling and was therefore masking. The observer, using a Frey hair easily felt in adjacent normal regions, tested centrifugally from the center of the masked area out toward its margin. The large areas of the forearm for each nerve were outlined before the more distal areas. The areas were measured by transferring each area to paper in paraffin duplicate and measuring it with a planimeter.

The results of the application of this procedure to the areas of sixty-five limbs of young adult males are analyzed statistically. The total area supplied by each nerve followed the normal curve in its variations from person to person. The "net total" cutaneous area of the forearm and hand also appeared to vary normally. The frequency distributions of the logarithms of the overlap areas likewise approximated the normal in their distribution.

The areas supplied by the nerves of the forearm, as would be expected, exceeded those supplied by the nerves of the hand. The overlaps between the nerves of the forearm were largest; next came two hand-forearm overlaps, then the overlaps between the nerves of the hand, and finally a group of much smaller hand-forearm overlaps. There was no significant difference between the mean values of the right and left areas supplied by each nerve.

The main areas differed little in variability as judged by the coefficient of variation. No difference between the variability of any area on the right limb

and its variability on the left limb was established. The overlaps differed from the main areas in that they tended to increase in variability with decrease in size. The variability independent of limb size exceeded 50 per cent of the total variability and were greater for the smaller areas.

The correlation coefficients indicated that in their variations all the main areas were appreciably associated with variations in limb size. Correlation coefficients indicated significant association between the area supplied by a nerve on the right limb and that on the left limb, as would be expected from the previous comparisons between the two sides.

The authors conclude that their technic is reasonably reliable for main areas and for large overlaps. Serious technical difficulties were experienced only in outlining the area supplied by the superficial branch of the radial nerve.

CHORNYAK, Philadelphia.

Physiology and Biochemistry

REACTIONS OF PATIENTS WITH INFANTILE PARALYSIS TO AUTONOMIC DRUGS. JOHN A. TOOMEY, Am. J. Dis. Child. **47**:573 (March) 1934.

To determine whether the sympathetic nervous system is involved in cases of poliomyelitis and whether this involvement is segmental, Toomey gave injections of pilocarpine and epinephrine hydrochloride to ninety-five patients suffering from unilateral paralysis. Pilocarpine hydrochloride was first administered, 1/10 grain (0.0064 Gm.) subcutaneously. If the sweating over the segmented areas of the paralyzed somatic nerves is more prompt, more severe or more persistent than on the healthy side, the reaction to the pilocarpine test is designated positive. Ninety-one of ninety-five patients showed positive responses to the pilocarpine test. One-half hour later an injection of epinephrine hydrochloride was given, 0.1 mg. intravenously or 1 mg. subcutaneously. If this results in disappearance of sweating on the normal side and persistence on the paralyzed side, the reaction is designated positive. Of forty patients seen early in the course of the disease, thirty-nine gave positive responses to both pilocarpine and epinephrine tests; of those seen later in the course of the disease, half gave positive reactions to the pilocarpine test and negative reactions to the epinephrine test. From these experiments the author concludes that the sympathetic nervous system is involved in segmental fashion and that it is involved as early as the somatic system.

DAVIDSON, Newark, N. J.

THE STORY OF THE DEVELOPMENT OF OUR IDEAS OF CHEMICAL MEDIATION OF NERVE IMPULSES. WALTER B. CANNON, Am. J. M. Sc. **188**:145 (Aug.) 1934.

The evolution of the various concepts dealing with the final recognition of the chemical mediation of nerve impulses is interestingly traced. Beginning with the suggestions of Elliott in 1904 and culminating with the recent work on sympathin, the author himself has played a prominent rôle in establishing the groundwork of these concepts. With Dale's work in 1914 there was a definite intimation that acetylcholine mimics the action of parasympathetic nerve impulses, much as epinephrine mimics the action of sympathetic impulses. In 1921 the researches of Loewi and of Uridil and the author further strengthened the concept of chemical mediation. This led through the studies on higher vertebrates without any sympathetic system. The most recent developments concern the differentiation of sympathin from epinephrine and the suggestion that there are two kinds of sympathin. With the belief that the new facts may hopefully be applied in the direction of the central nervous system, it is suggested that between the neurons of the nervous system, as well as between outlying autonomic neurons and their effector organs, chemical agents of transmission intervene.

MICHAELS, Boston.

MOVEMENTS OF EYES UNDER COVER. FRANK H. RODIN and ROBERT R. NEWELL, Arch. Ophth. **12**:525 (Oct.) 1934.

Rodin and Newell were unable to find any record of the movements of the eyes under cover, i. e., what position the eyes assume when they are both covered and padded. The only positive finding known relative to this has been repeatedly observed, that in sleep the eyes move upward. In this experimental work, markers were placed on various parts of the eyeballs and on the skin just off the external canthi. Roentgenograms were taken of the eyes in various positions and compared with roentgenograms of the eyes padded or bandaged. The conclusions are: no change in the movements took place when one eye was padded; bandaging one eye caused definite convergence of the eyes in the primary position and some convergence in other positions; padding both eyes caused convergence in the primary position but little effect otherwise; bandaging both eyes caused definite convergence and definite limitation of movements in the horizontal directions.

The interpupillary distance when looking to the right or left, as a rule, differs from that in the primary position. It may show either convergence or divergence. When it is desired to limit the movements of an eye or of the eyes to a minimum, bandaging of both eyes is recommended.

SPAETH, Philadelphia.

EFFECTS OF DRUGS ON VESTIBULAR REACTIONS. ELLISON L. ROSS and AXEL OLSEN, Arch. Otolaryng. **18**:753 (Dec.) 1933.

The demand for some drug that will act specifically to reduce the irritability of the vestibular apparatus is great. For a long time general sedatives, such as bromides and opium derivatives, have been employed with some degree of success. The chief objection to these is that when a sufficient amount is prescribed to reduce vertigo the patient is incapacitated by the general depression. A number of drugs were studied, and there was only one drug that had any significant effect. Strychnine reduced the reaction. The drugs used were those acting on the cerebrum, sympathetic nervous system and spinal cord. Pentobarbital sodium was used to depress the cerebrum and caffeine to stimulate it. Cocaine and epinephrine were employed to stimulate the endings of the sympathetic nerves. The spinal cord was stimulated with strychnine. The reactions with pentobarbital sodium were variable. The drug often did away with the nystagmus entirely. With caffeine, in general, there was small reduction in the duration of nystagmus. Stimulating the sympathetic nervous system with caffeine and epinephrine give no results. Strychnine, stimulating the spinal cord, decreased the reactions obtained by both positive and negative stimulation. In twelve of sixteen average tests there was a decrease.

A series of animals with only one labyrinth were given drugs representing the common pharmacologic groups: pentobarbital sodium representing the cerebral depressants; caffeine, cerebral stimulants; cocaine and epinephrine, stimulants of the sympathetic nervous system, and strychnine, stimulants of the spinal cord. The change in the duration of the nystagmus after a standard rotation and quick stop was taken as the measure of the change in the irritability of the vestibular system. The cerebral depressants decreased the reaction. However, the estimated degree of general depression was as great as, or greater than, the decrease of vestibular reaction. Caffeine did not increase the reaction to any significant degree. Stimulation of the sympathetic nervous system by cocaine and epinephrine had no significant effect. Strychnine, stimulating the spinal cord, decreased the vestibular reaction approximately 20 per cent.

R. J. HUNTER, Philadelphia.

EFFECT OF THE CENTRAL NERVOUS SYSTEM ON RESPONSES TO LIGHT IN EISENIA FOETIDA, SAV. C. LADD PROSSER, J. Comp. Neurol. **59**:61 (Feb.) 1934.

That earthworms respond negatively in light of moderate and high intensities and positively in light of low intensity is known. Prosser, from a series of experiments on normal specimens, concludes that the higher the luminous intensity,

within certain limits, the more strongly negative are the reactions of the worms and the lower the intensity the more strongly positive. Operations were carried out on the brains of worms. They were left for twenty-four hours and then tested for response to light every day until they had completely regenerated. The operations consisted of: (1) removal of the entire brain, (2) separation of the two lobes of the brain by a median cut, (3) removal of one lobe of the brain and (4) severance of one pharyngeal commissure. Worms so treated or worms subjected to subnormal temperatures or given injections of nerve-depressant drugs over the brain showed a marked decrease in the percentage of negative responses to light. Subjection to supranormal temperatures and injections of nerve-excitant drugs over the brain gave an increase of negative responses to light. An attempt at localization of function in the brain of Eisenia was made.

FRASER, Philadelphia.

MYELOGENY OF THE CAT AS RELATED TO DEVELOPMENT OF FIBER TRACTS AND PRENATAL BEHAVIOR PATTERNS. W. F. WINDLE, M. W. FISH and J. E. O'DONNELL, J. Comp. Neurol. **59**:139 (Feb.) 1934.

The purpose of the investigation reported here was to determine what relationship exists between the time of appearance of more or less definitely determinable reflexes and the advent of myelinization of the central nervous system pathways employed by these reflexes. The body and vestibular righting reflexes of fetal cats were chosen. Their development has been reported earlier. For staining the sections, the Pal-Weigert and the Weil technic were used. The process of myelinization has just begun on the forty-second day of fetal life (80 mm.). This is seen at the rostral level of the vagus nerve in the position of the future medial longitudinal fasciculus. At 90 mm. the ventral funiculus of the spinal cord is myelinated. In the cuneate fasciculus there are also myelinated fibers, which do not run far. The intramedullary ventral rootlets contain a number of thin myelin sheaths. At 100 mm. the cochlear nerve appears to lack sheaths entirely, but the vestibular nerve is one of the most heavily myelinated. A small direct vestibulospinal tract is identified. The spinal tract of the trigeminal nerve is well myelinated at from 110 to 120 mm. At 130 mm. the afferent facial nerve and the optic and cochlear nerves are myelinated. The appearance of myelinated fibers is shown in a convenient chart. The sequence of myelinization of fiber tracts and the order of the first appearance of their axons in the embryo, as previously reported by Windle, are in a general way correlated. It has been demonstrated that vestibular function begins to appear in some fetuses 110 mm. long. The vestibular nerve fibers and secondary vestibular pathways are myelinated in 110 mm. fetuses. There is a high degree of reflex activity possible in fetuses smaller than 80 mm. long, but even in the fetal cat near term (130 mm.) a distinct myelinated pathway for impulses mediating the body righting reflex is nonexistent. The authors conclude that myelinization is not correlated with function in an absolute sense.

ADDISON, Philadelphia.

THE FUNCTION OF THE BRAIN IN OLFACTION: II. THE RESULTS OF DESTRUCTION OF OLFACTORY AND OTHER NERVOUS STRUCTURES UPON THE DISCRIMINATION OF ODORS. H. G. SWANN, J. Comp. Neurol. **59**:175 (April) 1934.

The main olfactory structures of the brain of the rat constitute perhaps two thirds of the total cortex. The technic for testing olfaction in rats consisted of a simple discrimination between two odors. Extensive controls of cues foreign to olfaction were made, such as enucleation of the eyes. Taste did not seem to be involved, for after complete excision of the olfactory bulbs the animals showed no ability to discriminate. Forty-five rats were trained until there were twenty-seven correct responses in thirty consecutive attempts. After learning, the rats were rested for fourteen days and then retested for retention of discrimination by retraining to the same criterion. A part of the cortex was then destroyed by

electric cautery, and the animals were allowed fourteen days to recover before they were again retrained to the criterion of discrimination.

Destruction of the various parts of the archipallium or of the main fibers to and from the archipallium resulted in no significant harm to the retention of the olfactory habit. In a single case 39 per cent of the cortex was destroyed without loss of retention, whereas in Lashley's experiments a loss of 39 per cent of the cortex caused serious damage to maze-running ability.

The lateral and medial olfactory tracts were removed without serious loss in performance, but any interference with the anterior limb of the anterior commissure resulted in conspicuous loss of olfaction. This latter observation indicates that it is through this tract that the animal receives the nerve impulses used in this discrimination.

FRASER, Philadelphia.

THE INTRINSIC NERVOUS MECHANISM OF THE HUMAN LUNG. JOHN B. GAYLOR, Brain **57**:143 (June) 1934.

Gaylor presents a rather lengthy historical survey of the subject. The various aspects dealt with are: (1) the bronchial plexus, which is essentially a single plexus, ganglionated at certain of its nodes; (2) the epithelial innervation, which consists of sensory endings in the epithelium of the bronchus, in the plain muscle layer and in the pulmonary vessels; (3) the motor innervation of the bronchial musculature, and (4) the parent plexus of the vascular innervation of the pulmonary vessels. Of the more practical considerations, the suggestion is made that in addition to the mechanical difficulty of expiration in bronchial asthma there is a nervous upset. The possibility of axon reflexes is discussed.

MICHAELS, Boston.

THE PARTICIPATION OF THE NEUROGLIA IN THE FORMATION OF MYELIN IN THE PRENATAL INFANTILE BRAIN. BERNARD J. ALPERS and WEBB HAYMAKER, Brain **57**:195 (June) 1934.

From a study of the literature Alpers and Haymaker believe that there is good evidence that oligodendroglia cells and deposits of myelin are intimately related. Brains of premature infants ranging in age from 5 to 9 months were studied by means of specific stains for neuroglia. That the astrocytes probably play a part in the function of deposit of myelin about the axis-cylinder is shown by the presence of fat in the astrocytes during myelinization.

MICHAELS, Boston.

CHEMICAL TRANSMISSION OF THE EFFECTS OF NERVE IMPULSES. HENRY DALE, Brit. M. J. **1**:835 (May 12) 1934.

The effect of the transmitted impulses in nerve fibers is to awaken or to modify the activity of cells in relation to which the nerve fibers end. A study of this process has been one of the classic problems of physiology. Since the experiments of Claude Bernard it has been known that the location where the nerve fiber ends in the muscle has special physiologic properties. The impulse can be blocked by the administration of curare or by fatigue at this site even though the nerve itself and the muscle are still normally responsive.

The more recent theory that an excitatory substance is liberated at a nerve ending but destroyed within a few thousandths of a second might explain the known properties of a nerve ending. Experimental evidence is cited to show that there are two such chemical substances, acetylcholine or a choline ester and epinephrine. There appear to be cholinergic and epinephrinergic nerves. The former are the parasympathetic and the latter the true sympathetic nerves.

There is evidence that transmission at all cytoneural junctions is by the liberation of chemical transmitters, but in the case of motor nerves to voluntary muscles the experimental evidence is not as definite as in the case of the autonomic nervous

system. One receives an impression of the cholinergic mechanism as having the more general application in the functions of the nervous system, and probably an earlier origin in evolution, and of the epinephrinergic mechanism as a more specialized and probably a more recent development.

FERGUSON, Niagara Falls, N. Y.

ACTION OF ACETYLCHOLINE ON THE BRAIN AND ITS OCCURRENCE THEREIN. B. B. DIKSHIT, J. Physiol. **80**:409 (Feb. 28) 1934.

That parasympathetic and sympathetic nerves produce their effect by a specific chemical substance has been demonstrated by several workers. Evidence is presented in this paper which suggests that humoral transmission may occur in the central nervous system. Cushing found that injections of solution of posterior pituitary and of pilocarpine into the ventricles of the brain produced similar effects, although these two drugs produced totally different effects when given intravenously. He suggested that the drugs when given intraventricularly stimulated centers situated in the wall of the ventricles. This work suggested the possibility of vagomimetic drugs stimulating the vagal centers when injected intraventricularly, and Dikshit made experiments to compare the effects produced by central stimulation of the vagus nerve and intraventricular injection of acetylcholine.

Cats were used in all experiments. The vagus nerves on both sides were dissected and cut in the middle of the neck. It was found that electrical stimulation of the central end of the cut vagus nerve always caused complete cessation of respiration if a sufficiently strong stimulus was used. Acetylcholine was injected into the ventricles through a small hole trephined at the junction of the coronal and the sagittal suture. Actions produced by the mechanical effects of the injection were controlled by injecting an equal volume of saline solution before and after the injections of acetylcholine.

Dikshit found that injection of acetylcholine (from 0.1 to 1 microgram) into the cerebral ventricle of cats caused effects similar to that produced by stimulation of the central end of the vagus nerve, namely, arrest of respiration and occasionally cardiac irregularity. Intraventricular injections of this amount of acetylcholine did not produce a fall in blood pressure. The effects produced by intraventricular injections of acetylcholine were not affected by administration of large doses of atropine or of physostigmine. Extracts of the basal ganglia contained a depressor substance which showed the properties of acetylcholine in a variety of biologic tests. The cerebellum and cortex contained less of this substance than the basal ganglia.

ALPERS, Philadelphia.

THE PITUITARY GLAND IN RELATION TO POLYURIA AND TO WATER DIURESIS. W. H. NEWTON and F. H. SMIRK, J. Physiol. **81**:172 (May 21) 1934.

In 1929 Verney and his co-workers suggested the following hypothesis concerning water diuresis: The administration of water causes an inhibition of the secretory activity of the pituitary gland. The preformed pituitary hormone gradually disappears from the circulating blood, but for a time (about thirty minutes) is present in sufficient concentration to restrain the activity of the kidney. Fee (1929) performed experiments on decerebrated hypophysectomized dogs, removing from his preparations all tissue known to secrete pituitary hormone. He found that spontaneous polyuria did not develop in these dogs and that a dose of water caused, after an initial delay, a diuresis which ceased when the excess of water was excreted. From this experiment it seems at first sight that the renal excretion of water may be controlled normally in the absence of any tissue known to be capable of secreting the pituitary hormone.

According to the hypothesis, the decrease in the rate of formation of urine which takes place when an excess of administered water is excreted is due to the secretion of an antidiuretic hormone by the pituitary gland. In the absence of this hormone a state resembling diabetes insipidus should be produced. Yet despite

the absence of the pituitary gland in Fee's preparations, the rate of the formation of urine returned to normal after excretion of the excess of water. But before interpreting this observation one must know if diuresis has ceased physiologically or because the animal is incapable of a water diuresis. Newton and Smirk designed their experiments to overcome these and other difficulties in interpretation.

The experiments were made on cats and involved decerebration, with removal of the pituitary body, collection of urine and administration of water. Spontaneous polyuria occurred in about half of their experiments at times which varied from one-half hour or less to five hours after hypophysectomy. This increase in the flow of urine usually ceased spontaneously within from one to three hours without serious depletion of the animal's water reserves. When spontaneous polyuria did not occur, a dose of water was given and in most cases diuresis resulted, indicating that the kidneys themselves were still capable of water diuresis. It was found that when diuresis was absent after water was given this was often due to failure of alimentary absorption, but also that animals with satisfactory blood pressure and apparently in good condition might absorb water and yet have no subsequent increase in the rate of the formation of urine. In most animals, however, absorption of water was followed after a delay by the usual rapid increase in the flow of urine, succeeded by a decrease when the greater part of the excess of water was excreted. It is evident, therefore, that in these preparations there is nothing inherently adverse to water diuresis but sometimes unknown adverse factors are added which prevent the normal response to the administration of water.

In fifteen instances the administration of water was followed after a delay by what appeared to be typical water diuresis. In no case was the main increase in the rate of the formation of urine immediate, the average delay before the onset being forty minutes, the time taken to reach the peak of diuresis averaging one hundred and twenty-six minutes. The volume of urine excreted was less than the amount of water given and averaged 70 per cent.

The question as to whether this control of the elimination of water is truly physiologic is in part answered by five experiments in which absorption as well as excretion was recorded. In the course of these five experiments the authors gave twelve doses of water and obtained twelve periods of diuresis. On ten occasions attempts were made to measure the times absorption of water occurred and the measurements appeared to be satisfactory in eight of these attempts. In all of these eight instances the rate of formation of the urine was only just beginning to increase at a time when absorption of water was thought to be complete. In all eight instances the changes in the rate of the formation of urine lag behind the changes in the water load (i. e., the load of absorbed but as yet unexcreted water), often by as much as twenty minutes. In all of fifteen instances the increase in the rate of the formation of urine from the commencement of diuresis to the maximum flow of urine was gradual, not immediate, and lasted on an average for eighty-five minutes.

In all of fifteen instances when a sufficient time was allowed the rate of the formation of urine was observed to return toward normal on excretion of the greater part of the water given. In eight of these instances another period of diuresis was obtained after the first period subsided, showing that the cessation of diuresis after the first dose of water was physiologic in that the kidneys were still capable of diuresis. In all of six instances in which the previous exhibition of diuresis had demonstrated the capacity of the kidneys to show water diuresis there was still a delay between the absorption of a second dose of water and the resulting diuresis; also the increase in the rate of the formation of urine to its maximum was gradual, not immediate. This indicates that the delay in the onset of diuresis and the slow increase to a maximum in the rate of formation were natural and not due to progressing recovery of the preparation from the anesthetic and from decerebration. Six instances occurred in which in the interval of time between two successive periods of diuresis the rate of the formation of urine had fallen to within normal limits. The fact that diuresis after water occurs both before and after this interval indicates that the capacity of the kidneys to show a

water diuresis was probably satisfactory at the time. Yet, despite the absence of the pituitary gland, the rate of the formation of urine was then normal. It was observed on several occasions that the urine formed during diuresis was pale and poor percentually in urea and chlorides. The flow was reduced by administering ether or chloroform to the preparation. Fee observed in his experiments that the diuresis was curtailed by injections of a hormone of the posterior lobe of the pituitary gland.

Newton and Smirk conclude from their results that the pituitary gland and that part of the brain lying above the tentorium, which includes the hypothalamus, are not indispensable parts of the mechanism responsible for controlling water diuresis.

ALPERS, Philadelphia.

THE "WEVER AND BRAY PHENOMENON": A STUDY OF THE ELECTRICAL RESPONSE IN THE COCHLEA WITH ESPECIAL REFERENCE TO ITS ORIGIN. C. S. HALLPIKE and A. F. RAWDON-SMITH, J. Physiol. **81**:395 (June) 1934.

The experimental work described in this paper has been directed toward the solution of the problem of the origin of the cochlear effect. Hallpike and Rawdon-Smith have succeeded in confirming Adrian's suggestion that the abolition of the response in the auditory nerve consequent on its section is due to concomitant interruption of the vascular supply of the internal ear. It is possible in favorable preparations to divide the nerve without significant injury to the internal auditory artery, this lying in a well defined connective tissue strand anterior to the nerve. If this is done, the response from the central end of the cut nerve persists but disappears promptly when the vascular strand is divided.

The authors next studied the relative amplitude of the potentials developed in response to tones of high and low frequency, between an indifferent electrode in the muscles of the neck and a differentiated electrode making contact with (*a*) various points on the surface of the cochlea and (*b*) various points within the cochlea. The evidence adduced indicates, first, the good electrical insulating properties of the bony capsule of the internal ear and, second, that the responses from the apical and basal parts of the interior of the cochlea show marked differentiation for frequency, the low tone response being accentuated at the apex and the high tone response at the base. This is considered by Hallpike and Rawdon-Smith to constitute strong evidence of a direct nature in favor of the hypothesis that the cochlear elements are differentially tuned.

Although none of the evidence derived from these experiments is considered decisive in assigning to the cochlear effect a neural or non-neural origin, the authors believe the balance of the evidence favors a nonneural hypothesis.

ALPERS, Philadelphia.

THE EFFECTS OF SYMPATHETIC STIMULATION AND OF ADRENALINE ON MUSCLE GLYCOGEN. A. B. CORKHILL, H. P. MARKS and S. SOSKIN, J. Physiol. **83**: 1 (Dec. 14) 1934.

The recent evidence that epinephrine causes a breakdown of the glycogen of the muscle to lactic acid led Corkhill, Marks and Soskin to test whether stimulation of the sympathetic nerves to the muscles of the limbs can also produce this effect. The spinal eviscerated cat preparation was used, and determinations of muscle glycogen were carried out according to the dissection method of Best, Holt and Marks (1926). It is generally assumed that ergotoxine abolishes the motor effects of epinephrine and of stimulation of the sympathetic nerves. In particular, there is good evidence that epinephrine fails to produce a hyperglycemia in the presence of ergotoxine, and it might therefore be expected that its effect in discharging muscle glycogen would also be affected by ergotoxine. The action of ergotoxine was therefore included in the present study.

The experiments with stimulation of the sympathetic nerves have shown that this causes a definite though small decrease in the amount of muscle glycogen.

The results were rather irregular. In some experiments, though the signs of effective stimulation of the sympathetic nerves of plain muscle were clear, no definite change in the glycogen of the muscles was demonstrated. In others the decrease of glycogen was limited to one or two muscles taken for analysis. In several experiments, however, there was a definite decrease in all. It seems also that ergotoxine abolishes this effect, but since only two experiments with ergotoxine are available and since the effect, even without ergotoxine, may sometimes be negligible, the authors make this statement with due reservation.

The earlier experiments (Corkhill and Marks, 1930), in which epinephrine was administered in large amounts up to the limit of tolerance of the preparation, were supplemented by experiments in which smaller and more nearly physiologic doses were employed. These smaller doses produced a proportionately smaller, but still definite, discharge of muscle glycogen.

Since epinephrine and stimulation of the appropriate sympathetic nerves exert parallel effects on so many of the body structures, it is not surprising to find that they both give rise to a discharge of muscle glycogen. It is true that the discharge of glycogen produced by stimulation of the sympathetic nerves is on the average only about half of that produced by the administration of large doses of epinephrine, but this discrepancy might well disappear if one were able to determine the optimum frequency, wave form and duration of the stimulation to be applied.

The abolition of the effect of stimulation of the sympathetic nerves by ergotoxine is also in accordance with expectation; but it is not wise to stress the importance of this observation, since it is based on only two experiments. There is not sufficient evidence for endings of sympathetic nerves in the fibers of voluntary muscles. The effects of impulses from the sympathetic nerves on the glycogen content can on present evidence be regarded only as secondary to their action on the plain muscle of the blood vessels. Recent work, especially that of Cannon (1933), points to a chemical transmission of this action by release of a substance which, at least in its effects, closely resembles epinephrine. It would be natural, therefore, to attribute the effect on muscle glycogen to a leakage of this transmitter (Cannon's sympathin) onto the voluntary muscle fibers. Too little is known, however, as to this process to be able to offer any clear suggestion as to why the effect on glycogen of sympathin thus reaching the muscle fibers should be apparently annulled by ergotoxine while that of epinephrine reaching them from the blood vessels persists under the same conditions. There is a possibility that the sympathetic supply to the blood vessels of the muscles contains other adrenergic fibers and liberates, in addition, some other chemical transmitter which promotes the deposition of glycogen. If that were so, ergotoxine might swing the balance of effect from loss even to a small gain of glycogen, by a depressant action which, in the case of epinephrine alone, would be difficult to demonstrate in series of rather widely varying results. Such a possibility, however, could be discussed in definite terms only in the light of additional evidence.

ALPERS, Philadelphia.

VESTIBULAR FUNCTIONS OF THE FRONTAL LOBE WITH THE STRIATE BODY. CEREBRAL AND SUPRATENTORIAL ATAXIA. L. J. J. MUSKENS, Rev. d'oto-neuro-opht. **12**:117 (Feb.) 1934.

In this number Muskens discusses complications following the production of experimental lesions in the anterior part of the brain. The importance of the peculiar blood supply of the striate body is again emphasized. The cortex of the anterior part of the brain had been removed from an experimental animal. For months afterward it showed *mouvements de manége* toward the injured side. At autopsy a narrow area of softening in the pallidum and degeneration of the bundles going to the commissural nucleus and the substantia nigra were found. Since the anterior ascending fibers of the posterior longitudinal bundle decussate in the posterior commissure, it follows that in attempts at ablation of the frontal lobe or in cases of localized lesions of the striate body a concomitant lesion of the posterior longitudinal bundle is a troublesome complication. In the experimental

animals of Goll, Diesel and Morrison, in which the posterior longitudinal bundle system was injured, the resulting forced movements must be attributed to lesion of this system. The case of Gordon Holmes proves the predominance of the secondary vestibular system in case of a double lesion of the commissural system and of crossed lesion of the striatum. The researches of Diesel indicate clearly the effacement of the influence of the striatum with reference to secondary vestibular lesions and still more to primary vestibular lesions.

In the study of forced movements in inferior animals and mammals with horizontal vertebral columns an effort has been made to distinguish clearly between movements in the horizontal plane (*manège*) and those in the frontal plane (rotation). Great difficulties are encountered in making this distinction in animals with erect vertebral columns. It is comprehensible that in animals acquiring the erect posture the distinctive signs of forced movements and especially of the concomitant position of the eyes is lost. Often the two forced movements have been considered as being identical, differing only in degree. In physiologic experiments on animals different combinations of the two forced movements are observed: A lesion of the right vestibular nucleus causes rotation to the right and *mouvements de manège* to the right; a lesion of the posterior longitudinal bundle above the decussation of the vestibular fibers causes rotation to the right and *mouvements de manège* to the left; a lesion of the posterior commissure of the right side causes rotation to the left and *mouvements de manège* to the right. Physiologic experiments show also that the concomitant position of the eyes (strabismus of Magendie and Hertwig in cases of rotation, and conjugate deviation of the eyes in the horizontal plane in cases of *mouvements de manège)* as well as adequate positions of the trunk and extremities are also different.

DENNIS, San Diego, Calif.

APPEARANCE OF AN ACETYLCHOLINE-LIKE SUBSTANCE IN THE ADRENAL VEIN AS A RESULT OF STIMULATION OF THE SPLANCHNIC NERVES. W. FELDBERG and B. MINZ, Arch. f. d. ges. Physiol. **233**:657, 1933.

The blood of the adrenal vein of dogs and cats was collected before, during and after stimulation of the splanchnic nerves; by injection of physostigmine the property of normal blood to destroy acetylcholine was inhibited. The blood collected during stimulation of the splanchnic nerves caused contraction of muscles of leeches, which are very sensitive to acetylcholine. If this blood was injected into cats the blood pressure was changed in a way similar to that brought about by an acetylcholine-epinephrine mixture. It is concluded that acetylcholine appears in the adrenal vein if the splanchnic nerves are stimulated.

SPIEGEL, Philadelphia.

TULLIO'S ACOUSTIC REFLEXES. E. HUIZINGA, Arch. f. d. ges. Physiol. **234**:665, 1934.

Tullio observed movements of the head in pigeons in the direction of a semicircular canal on stimulation of the acoustic nerve after the osseous wall of the canal was opened. These observations are confirmed. The reactions are probably due to a stimulation of the crista. They persist after destruction of the cochlea but disappear if the external auditory canal is closed. They are probably not due to an increase of the excitability of the crista as Tullio assumed. The author explains the appearance of the reactions after the opening of the wall of the semicircular canal by the fact that sound waves elicit movements of the endolymph more easily under these conditions.

SPIEGEL, Philadelphia.

THE OXYGEN CONTENT OF THE CEREBRAL VEINS. P. BAMBERGER and H. E. NEVER, Arch. f. d. ges. Physiol. **234**:675, 1934.

The longitudinal sinus was punctured in infants with open fontanels, and the oxygen and carbon dioxide contents of this venous blood were determined by the

Van Slyke method. A comparison with the blood of the jugular, temporal and cubital veins showed that the blood of the cerebral veins contains less oxygen and more carbon dioxide than that of other veins.

SPIEGEL, Philadelphia.

ACTION CURRENTS OF THE STELLATE GANGLION AND OF THE DEPRESSOR NERVE. M. H. FISCHER and H. LOEWENBACH, Arch. f. d. ges. Physiol. **233**:722, 1934.

The action currents of the stellate ganglion and of the depressor nerve of the cat were recorded. In the stellate ganglion quick, biphasic impulses were observed at irregular intervals. They had no sure relation to the phases of the heart's action. The oscillations led off the depressor nerve appeared during each beat of the heart in three groups. In accordance with the observations of Bronk, the authors find that the oscillations in the depressor nerve depend on the changes of pressure in the aorta.

SPIEGEL, Philadelphia.

ELECTROBIOLOGIC PHENOMENA IN THE CEREBRAL CORTEX FROM LIGHTING ONE EYE. M. H. FISCHER, Arch. f. d. ges. Physiol. **233**:738, 1934.

The action currents of the area striata of the cat and of the rabbit were recorded while a beam of light was applied to the contralateral retina. Single stimuli were less effective than rhythmic stimuli. The typical action currents usually developed gradually during stimulation. If the stimulation was continued for some time, periods of action currents alternated with periods without reaction. This is probably due to rhythmic changes of the excitability of the optic centers. Action currents were also recorded when both electrodes were placed on the area striata. The inference is drawn that the centripetal impulses reach different parts of this area not simultaneously.

SPIEGEL, Philadelphia.

ELECTRICAL PHENOMENA IN THE OLFACTORY CORTEX ACCOMPANYING SMELL SENSATIONS. BUN-ICHI HASAMA, Arch. f. d. ges. Physiol. **234**:748, 1934.

Oscillations of the electrical potentials in the medial and basal cortical areas were observed in rabbits when olfactory stimuli were applied. These oscillations continue when the stimulus ceases. The strongest action currents were led off from the medial part of the lobus hippocampi. Subcutaneous injection of strychnine increased the effect, while application of cocaine to the nasal mucous membrane lowered it.

SPIEGEL, Philadelphia.

INVESTIGATIONS OF THE MOTOR CONSTITUTION. G. MARINESCO and A. KREINDLER, Arch. f. Psychiat. **101**:603 (Dec.) 1933.

Marinesco and Kreindler have attempted to investigate differences in certain physiologic motor functions by means of determinations of chronaxia and the development of conditioned reflexes in the different types of physical make-up. They found that the chronaxia, under ordinary conditions, did not show any consistent differences in the three types described by Kretschmer (pyknic, athletic and asthenic). However, the reactions of persons of these types following fatigue seemed to show definite specific tendencies. Similar significant differences could be found in the chronaxia following stretching of the muscles and also in the establishment of certain types of conditioned reflexes. They have also studied patients with hyperthyroidism and hypothyroidism and compared their reactions with those of persons of different types of physical make-up. They summarize their findings as follows: 1. The pyknic person shows a steep chronaximetric fatigue curve with a slow return to normal. A similar curve is observed for patients with hypothyroidism. The irritability of the muscles does not seem to be influenced by stretching. Motor conditioned reflexes tend to develop inhibition slowly, whereas vasomotor conditioned reflexes seem to be established more easily than the motor. 2. The athletic person has a steep chronaximetric fatigue curve.

but recuperation is faster than in the pyknic person. The irritability of the muscles is much influenced by stretching. Motor reflexes are only slowly inhibited, whereas vasomotor reflexes are established much more quickly than the others. 3. The asthenic person has a nearly flat chronaximetric curve, with a quick return to normal. Muscle irritability is increased by stretching; the motor conditioned reflexes are easily inhibited, and vasomotor conditioned reflexes are established more easily than the others.

MALAMUD, Iowa City.

THE PATHOLOGY OF THE EXCHANGE OF SUBSTANCES BETWEEN THE BRAIN AND THE REST OF THE BODY. V. KAFKA, Arch. f. Psychiat. **101**:231 (Dec.) 1933.

In order to understand the pathologic conditions in the exchange of substances between the brain and the rest of the body one must appreciate the limits of physiologic deviations. It has been shown that the exchange of substances between the brain and the body is increased in early infancy and in senescence as compared with normal adult life. Furthermore, whenever the concentration of a certain substance is increased in the blood there is also a tendency toward an increase of this substance in the cerebrospinal fluid. Pathologic changes may occur in a number of abnormal states. They can be produced by a change in the concentration of substances in the blood. In diabetes, for instance, the sugar content is increased not only in the blood but also in the cerebrospinal fluid. Disturbances occur in cases of disease of the glands of internal secretion; there is an increase of albumin in the blood and spinal fluid in myxedema. Similarly, activation of the reticuloendothelial system may change this function. Changes in permeability may also occur as a result of disturbances of the regulation of this process by the central nervous system. Finally, disturbances occur in diseases of the meninges, the brain, the capillaries of the brain and the choroid plexus.

In consideration of what is known at present of physiochemical laws regulating the exchange of substances through semipermeable membranes, it must be stated that the entrance of substances into the central nervous system cannot be altogether explained on that basis and a certain unknown biologic factor must be postulated. The anatomic substrates of the exchange of substances between the blood and the cerebrospinal fluid must be looked for in the plexus and in the endothelium of the meningeal vessels. Kafka is of the opinion that there is no sufficient proof for the assumption that a barrier exists between the cerebrospinal fluid and the brain and between the brain and the cerebrospinal fluid. On the other hand, definite evidence exists to support the view that such a barrier is interposed between the blood and the brain tissue. Finally, the assumption that the cerebrospinal fluid is the only nutritive agent for the central nervous system is not justified. Although the cerebrospinal fluid does serve this purpose the blood must be considered as playing an important rôle in this function.

MALAMUD, Iowa City.

Neuropathology

MOBILE SPASM OF THE NECK MUSCLES AND ITS PATHOLOGICAL BASIS. O. FOERSTER, J. Comp. Neurol. **58**:725 (Dec.) 1933.

A case of bilateral symmetrical spasm of the neck, with postmortem observations, is presented in support of Foerster's belief that spastic torticollis is a localized hyperkinetic condition limited to the muscles of the neck and due to an organic lesion of the neostriatum. The basal ganglia and the brain stem were examined in serial sections. Symmetrically placed lacunae, often of macroscopic size, were seen in all the ventral levels of the basal ganglia, particularly in the region of the anterior commissure. The lacunae occupied the putamen and the gray substance beneath the lenticular nucleus, the so-called substantia innominata of Reichert. Microscopically, in the tissue between the lacunae the perivascular spaces were seen to be considerably dilated. This état criblé was found through-

out the substantia innominata, the basal, medial and posterior parts of the nucleus lentiformis and the claustrum and in some of the adjacent convolutions of the insula. Around the lacunae and in the tissue showing the état criblé, ganglion cells were absent or sparse, while the glia cells were increased in number. The large lacunae probably originate from confluence of a number of smaller perivascular lacunae. This must be considered a pathologic condition and the process as due to a vascular condition.

ADDISON, Philadelphia.

A CEPHALIC MONSTER: AN UNUSUALLY LARGE MENINGO-ENCEPHALOCELE. DAVID T. DUBOW and FRANK M. KRAMER, Psychiatric Quart. **8**:288 (April) 1934.

What is believed to be the largest meningo-encephalocele on record is here reported. The baby weighed 6 pounds (2.7 Kg.) at birth and lived for nine days. It did not cry and scarcely moved during its short life. The sucking reflex was incompletely developed, but the pupillary response was normal. A large saclike structure, measuring 11 by 12 by 6 cm., was attached to the posterior fontanel and covered by an extension of the scalp. Within the cranium the brain showed an accessory lobe at the sylvian fissure. The cranial nerves appeared to be anatomically normal, except that the olfactory nerves could not be found. The right cerebellar hemisphere was vestigial. The sac contained almost 400 cc. of blood-stained fluid, in which were floating some round embryonal cells and a moderate quantity of cholesterol. In the sac there were two masses of brainlike tissue, one continuous with, and apparently an extension of, the occipital lobe. In the other, the cortex and white matter were inverted in their relative positions. Both masses had convolutions, and each was covered by a pialike membrane. A large ventricle was common to the two masses. No choroid plexus tissue was found. The histologic pictures of the intracranial and extracranial brains were identical. The individual neurons were poorly developed, small and elongated. Many unipolar spongioblasts and immature glia cells were seen.

DAVIDSON, Newark, N. J.

SENILE PLAQUES. L. BOUMAN, Brain **57**:128 (June) 1934.

Bouman describes four groups of alterations typical of senile dementia: (*a*) torpedoes (local spool-like swellings) of the neurites of some of the Purkinje cells; (*b*) Alzheimer's type of fibrillary change in some of the ganglion cells of the cerebral cortex; (*c*) knots, buds, eyes and a splitting up of the neurofibrils in some neurites near or in a senile plaque, and (*d*) senile plaques are described in detail. By considering the characteristics common to these the author believes that knowledge as to their common cause may be obtained. "Hyperdifferentiation" is the single term which may be applied to the four histologic alterations mentioned. If this process occurs in a ganglion cell the Alzheimer type of fibrillary alteration results; if in a neurite, a torpedo is formed; if in dendrites, dendritic swellings develop; if in neurites from a senile plaque, knots, buds, eyes and argyrophil fibers result; if in the nondifferentiated protoplasmatic ground reticulum of the nervous system, a senile plaque is formed. The genesis of the changes described remains unknown.

MICHAELS, Boston.

SUBACUTE SPINO-CEREBELLAR DEGENERATION OCCURRING IN ELDERLY PATIENTS. J. G. GREENFIELD, Brain **57**:161 (June) 1934.

Greenfield reports two cases of spinocerebellar degeneration. In one case, that of a woman, aged 66, the illness lasted three months, and in the other, that of a man aged 57, the illness lasted seven months. The outstanding symptoms, in addition to pains and weakness in the limbs, were those indicating involvement of the cerebellum. Degeneration of the long tracts of the cord, especially the dorsal columns and cerebellar tracts, with earlier degeneration of the pyramidal tracts was found. There was a gross loss of Purkinje cells, and in the nucleus of Luys

the strioluysial fibers were degenerated, and there was fairly intense perivascular infiltration in the neighborhood of degenerated tracts. The latter observation was reflected in the cerebrospinal fluid. The relationship to parenchymatous cortical cerebellar atrophy and olivopontocerebellar atrophy is discussed.

MICHAELS, Boston.

CEREBRAL STRUCTURE AND MENTAL FUNCTION AS ILLUSTRATED BY A STUDY OF FOUR DEFECTIVES' BRAINS. R. J. A. BERRY and R. M. NORMAN, J. Neurol. & Psychopath. **14**:289 (April) 1934.

Detailed histologic study of the cortical architecture of the brains of three imbecilic and one feebleminded person revealed that the number of supragranular and granular neurons was significantly reduced, although the total depth of the cortex was not appreciably diminished except in the agranular frontal cortex; the cells were irregularly arranged, tended to be smaller than normal and were often of abnormal shape and staining property. As macroscopic examination also revealed insufficient gyral development, these changes are believed to be of prenatal origin and to be directly related to the functional mental states of the patients. This is suggested by the more normal arrangement and shape of cells of the cortex in the feebleminded person. An associated diminished size of the corpus callosum is corroborative of a general lack of development of the central nervous system.

SPERLING, Philadelphia.

CONTRIBUTION TO THE STUDY OF THE HISTOPATHOLOGY OF RETINITIS PIGMENTOSA. E. REDSLOB, Ann. d'ocul. **170**:1040 (Dec.) 1933.

From pathologic examination in cases of retinitis pigmentosa Redslob concludes that the disease is in reality chorioretinitis. The primary lesions are caused by chronic inflammatory processes in the inner layers of the choroid. The inflammatory process destroys the sensory cells. This, in turn, causes the pigmentation of the retina, because the connective tissue which is formed penetrates the retinal tissue, carrying with it proliferating pigmented epithelium of the retina.

BERENS, New York.

ANATOMIC AND PATHOGENIC CONSIDERATIONS OF THE MYOPATHIES. R. POINSO and Y. POURSINES, Rev. franç. d'endocrinol. **12**:357 (Oct.) 1934.

Poinso and Poursines report a clinical and anatomic study of a case of the Leyden-Moebius type of myopathy and discuss the various pathogenic theories, especially the autonomic-endocrine. The case is that of a boy who began to have difficulty in walking at the age of 10. Six years later he was bedridden, with contractures in flexion in both lower extremities and the feet in the equinovarus position. Except for the right ankle jerk, all deep and superficial reflexes in the lower extremities were abolished. The motility in the upper extremities was greatly reduced, and there was atrophy of the left thenar group. The deep reflexes were abolished in both arms. The electrical reactions were decreased in all the affected muscle groups. There were no fibrillations or sensory changes. About three months prior to death hard masses appeared in the breasts and numerous small nodules under the skin of the abdomen, chest and neck. Coincident with this the patient began to lose weight rapidly. There was also enlargement of the liver and of the left testis. Autopsy was performed a few hours after death. The skeletal muscles were pale and reduced in volume. No trophic changes were present in the musculature of the heart and intestines. There was invasion of an epitheliomatous tumor mass into the pancreas, spleen, liver, right adrenal gland, testes, lungs and intestines. Histologic study of the striped musculature revealed some changes in the transverse striation, nuclear proliferation, formation of sclerotic tissue, sclerosis of the sarcolemma and of the interstitial tissue and collagenous metaplasia of muscle fibers. No young muscle cells or vacuoles

could be seen in the preparations. The spinal cord showed changes in the cervical, lumbar and sacral segments. Some of the motor cells of the anterior horn were enlarged, and the basophilic substance was increased. In the intermediolateral process of the column of Clarke there were changes consisting of hypertrophy of the cells with displacement of the nucleus and transformation of the nuclei into a homogeneous substance which stained pale blue with toluidine. In addition, there were some periependymal proliferation and thickening of the arachnoid. The rest of the central nervous system showed no evidence of change.

The authors review the various pathogenic theories. They think that the diminution and abolition of the tendon reflexes and the changes in the electrical reactions in their case speak in favor of an etiologic origin in the spinal cord, and in support of this they emphasize the pathologic changes in the spinal cord. They refer to the occasional combination of postencephalitic parkinsonism with the syndrome of myopathy as described by Tinel, Schiff and Courtois, and to the degenerative changes in the striatal system and the subthalamic region as found by Foix and Nicolesco. Then they discuss the theory of primary muscular involvement as advanced by Charcot, Landouzy, Dejerine and others. Finally, the authors discuss the endocrine theory postulated by Claude, Langeron, Dragonesco and others, who emphasized the combinations of myopathy with hypertrophy of the thyroid gland, hyperpituitarism or hypopituitarism and adrenal insufficiency. As they noted definite changes in the intermediolateral process of the column of Clarke in their case and as this structure has vegetative autonomic functions, the authors believe that their observation substantiates the vegetative-endocrine pathogenic theory of myopathy.

NOTKIN, Poughkeepsie, N. Y.

PATHOLOGIC CHANGES IN THE NERVOUS SYSTEM IN POSTDIPHTHERITIC NERVOUS DISEASES. B. HECHST, Arch. f. Psychiat. **101**:1 (Nov.) 1933.

Some authors believe that the primary lesion in the nervous system in cases of diphtheria is in the peripheral nerves; others believe that it is in the spinal cord cells, and still others, that it is in the blood vessels; finally, the muscles or the terminal connections between the nerves and the muscles have been thought to be the original site of the lesion. Hechst studied five cases, in two of which death occurred and autopsy was performed during the early stages of the disease, when there were no clinical signs of postdiphtheritic changes. He reaches the following conclusions: 1. Diphtheria causes changes in the ectodermal and mesodermal elements of the central nervous system. The mesodermal changes, however, do not seem to be of great importance in the determination of the degree of change in the parenchyma. 2. In some cases changes are found in the posterior tracts, apparently caused by lesions in the spinal ganglia. 3. The distribution of the histologic changes depends on three features: the points of entrance of the toxin, the duration of the disease and the specific affinity of special parts of the nervous system for the diphtheria toxin. 4. In the cases studied the greatest affinity toward diphtheria toxin was shown by the vagus, the nerve cells of the striatum and the spinal ganglia. 5. The seat of primary anatomic lesions in postdiphtheritic polyneuritis can be found at the centers as well as in the periphery.

MALAMUD, Iowa City.

HISTOPATHOLOGIC INVESTIGATIONS OF THE SO-CALLED SCHIZOPHRENIC FORM OF DEMENTIA PARALYTICA. B. HECHST, Arch. f. Psychiat. **102**:35 (April) 1934.

Hechst examined histopathologically the brains of three patients with dementia paralytica, who had presented a clinical picture very much like that seen in cases of schizophrenia. He was particularly interested to see whether histopathologic differences existed between these schizophrenic forms and the usual types of dementia paralytica, especially with reference to the light that might be thrown on the histopathology of schizophrenia. The results were: 1. No particular similarity was discovered between the areas involved in these cases and those which have

been described as affected in cases of schizophrenia. There was, however, little if any involvement of the subcortical ganglia. 2. In contrast to the types of changes usual in cases of dementia paralytica which follow the typical clinical course, the intensity of the changes in these cases was much attenuated. 3. There was no distinct difference in quality between the histologic changes in these cases and those usual in cases of dementia paralytica. 4. In view of the fact that pronounced auditory hallucinations were present in these three cases, and because it has previously been claimed that in cases of dementia paralytica with auditory hallucinations there is a marked involvement of the temporal lobes, these areas were particularly carefully studied; no such relationship could be discovered.

The author comes to the conclusion that if there are any characteristic features in this type of dementia paralytica they consist in an attenuation of the intensity of the cortical process and in an intactness of the subcortical ganglia.

MALAMUD, Iowa City.

Psychiatry and Psychopathology

THE RELATION BETWEEN ORAL AND RECTAL TEMPERATURES IN NORMAL AND SCHIZOPHRENIC SUBJECTS. HUGH J. CARMICHAEL and FOREST C. LINDER, Am. J. M. Sc. **188**:68 (July) 1934.

This investigation was carried on to determine more accurately the relationship between the oral and the rectal temperature in twenty-five schizophrenic male subjects and twenty-four normal male subjects. Although the mean difference between the oral and the rectal temperature in the normal subjects was 0.95 degree, the average difference in individual subjects of the group ranged from 1.79 to 0.42 degree, and hence predictability becomes impossible. The mean oral temperature was 0.54 degree lower than the rectal temperature in the schizophrenic group; the average difference in individual subjects ranged from 0.8 to 0.26 degree. In the normal group individual correlation coefficients average + 0.56; in the schizophrenic group, the average was + 0.73. The difference in the figures for the groups may be in part accounted for by the greater activity of the "normal persons."

MICHAELS, Boston.

TUBULAR VISION. RALPH C. HAMILL, Arch. Ophth. **12**:345 (Sept.) 1934.

Disturbance of vision and hearing can be considered from the side of mechanics or from that of mentality. If a patient complains of disturbances of vision the fault may be with his personality and his assertions rather than with his visual apparatus. As sensation depends on the proper functioning of three components—a receiving apparatus, a transmitting line and a recording consciousness—disturbances in sensation may result from disturbances of any one of these three components. A receiving apparatus and a transmitting line acting on physical and mechanical conceptions are free from moralistic quality or taint; a recording consciousness not yet reduced to physical terms is still of a spiritual quality and of necessity has, like all things spiritual, a moral tone.

The importance of the attitude factor is seen most clearly in the condition called hysteria. The anesthesias and analgesias of hysteria are notorious. Hysteria is a state of disability that demands and so discovers physical symptoms. The hysterical person and his physically minded physician have the same end in view: Both do their utmost to see the disability of the patient in physical terms, dependent on physical disease. Tubular vision is a characteristic condition in hysteria. At least, concentric limitation of the field of vision is common, and tubular vision is a concentric contraction which remains unaltered in extent when the patient is examined at different distances from the fixation point.

Three cases are reported in detail as illustrations.

SPAETH, Philadelphia.

PARENT CHILD RELATIONSHIP IN SCHIZOPHRENIA. J. KASANIN, E. KNIGHT and P. SAGE, J. Nerv. & Ment. Dis. **79**:249 (March) 1934.

A series of forty-five unselected cases of schizophrenia were studied for the presence of parental overprotection. This was found in 60 per cent of the cases. Rejection by the parent was found in only two cases, with the evidence coming from the patients themselves. In cases of schizophrenia the authors found that overprotection frequently extends into the adult life of the patient and even into the hospital life after commitment. The physical and intellectual inferiority of some of these schizophrenic children is easily detected by the parents and serves as one of the principal causes of overprotection, which is solicited and invited by the preschizophrenic child. The overprotection establishes a vicious circle in the life of the schizophrenic child, because on the one hand the child needs the extra care for his development but on the other hand this extra care hinders his final development, which is his emancipation from his parents and his psychosexual development.

HART, Greenwich, Conn.

BACILLUS TUBERCULOSIS IN PSYCHOTIC PATIENTS. NICHOLAS KOPELOFF and E. LOEWENSTEIN, Psychiatric Quart. **8**:72 (Jan.) 1934.

The blood of forty-two psychotic patients and twelve nonpsychotic control subjects was examined for tubercle bacilli by the Löwenstein method. The blood of twenty of the forty-two patients gave a positive culture of tubercle bacilli—an incidence of 48 per cent. From no specimen of blood of a control subject were the acid-fast bacilli cultured. The proportion of cultures that were positive for tubercle bacilli varied with the different psychoses; in cases of manic-depressive psychoses and psychoneuroses 50 per cent of the specimens were positive. Two patients with involution melancholia gave positive reactions. Thirty-four of the specimens came from schizophrenic patients, and of these fifteen gave positive responses.

DAVIDSON, Newark, N. J.

SOME PERTINENT PROBLEMS IN THE ADMINISTRATION OF PHYSICAL EDUCATION FOR THE MENTALLY ILL. JOHN E. DAVIS, Psychiatric Quart. **8**:158 (Jan.) 1934.

Suitable motivation is an important factor in psychic rehabilitation, and as the motivation toward play is instinctive and spontaneous, it offers a better starting point than many forms of work activity. A lowering of the instinct toward action is characteristic of many psychoses, notably schizophrenia, and getting the patient started represents a long step forward. Physical education is peculiarly suited to the duty of making this first step. The nature of the particular play activity prescribed should be determined not by the psychiatric diagnosis but by the patient's psychologic reaction type. Permitting the patient to handle the play objects is more effective than telling him what to do or discussing how it should be done. By providing a socially graded series of play activities the physical education director can see the patient advance from the stage of solitary play to a phase in which he plays in small groups, and then to a stage in which he plays noncompetitively in large groups, reaching eventually a phase of integrated, competitive, highly socialized play activity.

DAVIDSON, Newark, N. J.

THE OVEREVALUATION OF LOVE: A STUDY OF A COMMON PRESENT DAY FEMININE TYPE. KAREN HORNEY, Psychoanalyt. Quart. **3**:605, 1934.

Horney describes a type of woman with no prominent symptoms but whose main difficulty seems to be inability to establish a satisfactory desirable relationship with men, an inhibition in the sphere of work and accomplishment and a well marked impoverishment of interests. The central problem seems to be not an inhibition respecting love but a too exclusive concentration on men, so that by comparison all the rest of life lacks interest. The women of this type who

were studied showed a definite fear of not being normal. They presented a double discrepancy: There was an impulsive overevaluation of a heterosexual relationship and an underevaluation of their gifts, abilities, interests and ambitions, i. e., a displacement of emphasis from attainment or the struggle for achievement to sex. The transference situation to a woman analyst was dominated by two attitudes —rivalry and recourse to activity in relation to men. In regard to the latter, three tendencies came to the fore: (1) fear of dependence on a woman, (2) the use of jealousy to evoke the analyst's love and (3) a spiteful attitude to the analyst. Such a situation might seem to be based on a strong yet dreaded homosexuality, but such interpretations were ineffectual therapeutically. In the homosexual woman the decisive factor lies in a very early and far-reaching resignation of men; their erotic rivalry with women recedes into the background, and there results a coupling of destructive and sexual impulses with a love which overcompensates these disturbing trends. In the type here described this overcompensation does not occur, and the rivalry persists and is sharply aggravated because the aim of the struggle, the obtaining of a man, has not been given up. In all the histories there was one factor which occurred regularly and with marked affect: All of the women had come off second best in competition for a man. In seven of the thirteen cases there had been an elder sister who was preferred by the father. The anger against the sister was centered on two points: (1) the sister's feminine coquetry (this prevented the patient's development by making her repudiate all feminine wiles), and (2) the sister's actual hostility to the patient (the sister did this by intimidating and ridiculing the patient and by making the patient sexually dependent on her). Also, in the majority of cases very early genital excitation had precipitated sexual development. Such premature genital excitation laid the foundation for an earlier appreciation of the importance of the struggle for possession of a man. This struggle brought in its train a permanent and destructive attitude of rivalry with women, with the psychology of the vanquished, i. e., a feeling of being downtrodden, a permanent feeling of insecurity with regard to feminine self-esteem and a profound anger and a marked death wish against more fortunate rivals. If the hatred of the victorious rival remains preconscious, the blame for the whole failure is placed on other women. If more deeply repressed, the reason for the lack of success is sought in the patient's own personality and self-blame. Another form of defense is the wish to be a man, and another the proof that she can attract a man; the latter is often seen as a frank pursuit of a man regardless of his other qualities.

Analysis reveals an anxiety concerning the sexual organs. The extreme defense against masturbation is founded on the antifemale sadistic fantasies the essential element of which is the wish to mutilate a woman's genitalia. The defense instituted against these aggressive fantasies, which appears as a resistance against analysis, is really a defense against the sense of guilt with the meaning of "I have not injured myself, I am made this way." The fantasies of masculinity do not represent the dynamically effective agency but are an expression of secondary tendencies which have their root in the rivalry with women, being both an accusation against the mother for not being born a man and an expression of the need to create a means of escape from the torment of feminine conflicts.

Although, so far, the overevaluation of relationships with men seems to have its source as a restoration of wounded self-esteem and defiance of the victorious female rival, it becomes necessary to inquire whether the desire for sexual gratification does not play an essential part. Sexual intercourse is important to these patients, and they assure themselves of it in three ways—prostitution fantasies, the desire to marry and the wish to be a man. The first two signify that there will always be a man available, and the third, the idea that a man can have intercourse when he wants it.

On the basis of the manifest clinical pictures presented, these patients run the gamut from women who are extremely inhibited in making advances in establishing relationships with men, although craving for them to the exclusion of all other wishes, to women of a Don Juan type.

The tendency to make a person dependent through love has another detriment, i. e., an anxiety that says dependence on any one must be avoided at all costs because it will result in the mistreatments that have been experienced in childhood. The patients have only one way out of this unsatisfactory situation, i. e., by achievement, esteem and ambition. But on these drives they are doomed to failure because of the rivalry situation and because of their Don Juanism (they are incapable of tying themselves down to any particular type of work).

Often in marriage such a woman transfers her ambitions onto her husband and then makes his success uncertain because of her unconscious expectation of his failure. Between her ambitions and her lack of self-confidence there is a striking discrepancy which paralyses activity and prevents her from living by practice because she expects to be able to excel in a technical procedure at once and cannot stand the test of failure. Thus she retains with tenacity the feeling of incapacity because it prevents her from entering into rivalry, and also because it subserves the positive desire to extort a man from fate by all costs, giving proof of her own dependence and helplessness.

The masochistic attitude is a neurotically distorted means of attaining a heterosexual goal. Since work must remain unproductive, unsatisfactory and actually painful, these patients are thrust back in a secondary manner on the erotic sphere. These difficulties become pronounced with increasing years. Dr. Horney believes that this type of woman, frequent in middle class intellectual circles, can result only from individual causes, but that given the present-day social factors relatively minor difficulties in personal development suffice to draw women in the direction of this type of womanhood.

PEARSON, Philadelphia.

PRINCIPLES OF PSYCHOTHERAPY AS APPLIED TO GENERAL PRACTICE. C. STANFORD READ, Brit. M. J. **1**:931 (May 26) 1934.

As its title suggests, this article is written primarily for physicians engaged in general practice. For many reasons the family physician is in a particularly advantageous position to utilize the principles of psychotherapy, primarily because of the trust bestowed on him and partly because he sees many of his patients with functional disturbances in the early stages of the condition. The ideal psychotherapeutist is said to be born, not made. He must be a man of the world, have wide interests and sympathies, be patient, be able to identify himself with his patients and possess a love of humanity and have not only an earnest desire to help but the firm conviction that somehow or other he will be capable of doing so. "Faith acts through suggestion." The first step in psychotherapy is to listen, by reason of which there is a cleansing of the mind. By careful questioning later, the physician further orients himself as to the severity of the neurosis, the type of personality with which he has to deal and the form of therapy indicated. Read thinks that there is too great a tendency for physicians to adhere to one form of therapy exclusively. In the simplest case of neurosis, a heart-to-heart talk, a little added insight, a little advice and some encouragement may be all that is necessary. In others, psychoanalytic therapy alone can promise results. There are many cases which fall between these extremes. Consciously or unconsciously, suggestion is used constantly. Not infrequently its value is either neglected or misused. It is closely related to hypnotism. It is of most value for highly suggestible persons. In old age, ideas are more fixed. It becomes somewhat contagious in a group. Anything which lessens cerebral control, such as alcohol and fatigue, increases suggestibility. A positive emotional relationship encourages it.

Read believes that hypnosis has been neglected too much since analytic therapy has come to the fore. It is of special value in the treatment of fugues, amnesia and dual personality. Occasionally the mere induction of hypnosis itself may do good, but usually direct or indirect suggestion given during the hypnotic state is responsible for its beneficial results. The indirect suggestion is generally more effective since no contrasuggestions tend to be formed. Just as good results can frequently be obtained through suggestion in the waking state if the patient is in a condition

of absolute passivity of body and mind. The validity of autosuggestion is questioned. When it has seemed successful, the personal influence was exercised through the reading of a book or through repeating of phrases previously spoken by a physician. The results of suggestive therapy are variable. At times they may appear miraculous, but cured patients are often only seemingly cured and have relapses later. Its great disadvantage is its blind nature and the fact that it should be used only when for any reason a more scientific and analytic approach is not feasible.

In persuasion therapy it is presumed that if the meaning and origin of symptoms are explained the patient has the capacity to modify morbid mental processes. Logical reasoning, however, has little power to modify what goes on in the mind; those who can be helped in this way are comparatively few in number. A more rational approach is that of reeducation. If the physician is well equipped with modern psychopathologic knowledge, so that he is able to relate the past to the present, he may be able to modify the patient's attitude, render it more rational and give a new goal to life. In general practice this method will be most applicable to the majority of patients whom the family physician is called on to treat. It should be remembered, however, that by this method much pathogenic material in the unconscious mind remains untouched. In the early severe neurotic situations, psychoanalysis is the therapy recommended. Frequently too much is expected of the psychotherapeutist. "Just as we come across people with poorly developed chests who will always be liable to cough and who break down under respiratory strain, so we meet with a constitutionally poor mental soil that will ever be apt to find it difficult to withstand the stresses of life without developing symptoms of maladaptation." There are some persons who cannot be made normal but who can be helped to a better adjustment to life.

FERGUSON, Niagara Falls, N. Y.

Diseases of the Brain

ENCEPHALITIS IN CHILDREN APPARENTLY CONGENITAL AND FOLLOWING MATERNAL INFLUENZA. WINNIFRED BAYARD STEWART, Am. J. M. Sc. **188**:522 (Oct.) 1934.

Epidemic encephalitis complicating pregnancy is not so fatal to the pregnant woman or the fetus as is influenza. The cases of seven children born of mothers who had influenza during the later months of pregnancy are reported. Symptoms have apparently been present from the time of birth; no history of acute illness which might have been epidemic encephalitis was found. The children present character defects typical of postencephalitic behavior, and in five cases there was evidence of organic involvement of the extrapyramidal system. Although there is no definite proof in these cases of the existence of a common etiologic factor of the influenza in the mother and encephalitis in the child, it is suggested that such may be the case.

MICHAELS, Boston.

THE EFFECT OF CEREBRAL LIPOIDS ON THE BASAL METABOLISM IN GENERAL PARESIS. EMIL T. HOVERSON, Am. J. Syph. & Neurol. **18**:373 (July) 1934.

Variable basal metabolic rates were found in untreated and in heat-treated persons with dementia paralytica; of a group of untreated patients, 20 per cent had low and 46 per cent high metabolic rates; of a group treated with typhoid vaccine, 21 per cent had metabolic rates below normal and 35 per cent rates above normal; of a series of patients treated by induction of high fever with the electric cabinet, 22 per cent had rates below minus 10, and 44 per cent had rates above plus 20. Twenty-one of these patients then received tryparsamide and injections of cerebral lipoid. The injections were administered every other day until no further change in reaction was produced. This usually took from two to five weeks. The general effect of the treatment was to move the metabolic rate toward

normal. Thus, five patients who had minus metabolic rates before the regimen showed higher rates after it, three of them reaching plus rates. Fourteen patients who had plus metabolic rates before the program was instituted showed lower rates at its conclusion. Three rates were reduced to exactly zero and eight decreased to minus values and three to smaller plus values.

The author suggests that in cases of syphilis a disturbance of the oxidation-reduction process occurs within the cells, accounting for this metabolic variability as well as for the emotional instability. The cerebral lipoid, he believes, tends to stabilize the oxidation-reduction process, thus normalizing the metabolic rate and reducing the emotional instability of the patient. DAVIDSON, Newark, N. J.

RETINOBLASTOMA. MORRIS JAFFE, Arch. Ophth. **12**:319 (Sept.) 1934.

While numerous cases of retinoblastoma have been reported in the literature, complete reports of cases that came to autopsy are comparatively rare. The case which the author reports presented many points of interest. A Negro girl, 2 years of age, underwent enucleation of an eye a few days after a diagnosis of retinoblastoma had been made. The pathologic report showed a mass composed of small round cells, with little cytoplasm; the chromatin was dense and fragmented. The cells were arranged for the most part around blood vessels, with marked degeneration and necrosis away from the vessels. A few circular or tubular arrangements of tumor cells were present. There was no extension into the optic nerve. The diagnosis based on the pathologic picture was retinoblastoma.

Six months later the child was readmitted to the hospital with a large friable mass filling the right orbit. The left eye was normal, and ophthalmoscopic examination did not disclose any intra-ocular growth. There was a hard infiltrating mass within the mouth, which seemed to spring from the right side of the inferior maxilla. The tissues of the pharynx were edematous, and there was infiltration. The abdomen was distended. The liver was 3 fingerbreadths below the costal margin.

Postmortem examination showed several lumpy, soft tumors of the zygoma and the scalp. The lower maxilla had undergone complete necrosis near the right articulation. A tumor was present in the left temporoparietal region. The bones of the right orbit had undergone necrosis. The liver was one and a half times the normal size and was diffusely studded with soft white nodules of tumor tissue. The left ovary was involved. Even the skull showed areas of softening with small areas of tumor cells present.

The postmortem diagnosis was retinoblastoma originating from the right eye with metastasis to the skull, scalp, lymph nodes, liver, ovary and inferior maxilla.

SPAETH, Philadelphia.

THE NITRITE OF AMYL TEST FOR THE DIFFERENTIATION OF TUMORS OF THE BRAIN FROM VASCULAR AND CHRONIC INFLAMMATORY LESIONS: A. PRELIMINARY REPORT. CLARENCE C. HARE, Bull. Neurol. Inst. New York **3**:513 (March) 1934.

Former studies to determine the value of the amyl nitrite test as a diagnostic measure for spinal subarachnoid block showed a suggestive difference in manometric pressures in patients who had tumors of the brain and those who had vascular or chronic inflammatory lesions of the brain.

Hare presents comparative manometric readings taken after inhalation of amyl nitrite for three groups of subjects: 1. The first group consisted of eighteen patients with tumor of the brain; sixteen of these showed pressure readings between 330 and 520 mm.; two showed levels between 260 and 270 mm., and in these autopsy revealed cerebral tumors with extensive areas of softening. 2. The second group consisted of twenty-two patients with vascular lesions and eighteen with chronic inflammatory disease. Nineteen of the twenty-two patients with vascular lesions had a spinal fluid pressure which varied from 130 to 315 mm.; three

showed readings of 360, 400 and 455 mm., respectively; two of these subjects had a high degree of hypertension. Sixteen of the eighteen patients with chronic inflammatory conditions showed levels between 85 and 320 mm.; hypertension was present in the other two cases. 3. The third group consisted of fifty patients in whom there was no known organic disease of the brain. The results for this group are not included in the report.

Hare believes that the amyl nitrite test is of diagnostic value in differentiating between expanding lesions and vascular or inflammatory diseases of the brain.

KUBITSCHEK, St. Louis.

AN ANALYSIS OF DISTURBED FUNCTION IN CASES OF APHASIA. KONRAD ZUCKER, Brain **57**:109 (June) 1934.

A detailed examination in the case of a man, aged 43, who probably had a lesion of the left posterior temporal area due to posttraumatic hemorrhage, is presented from the point of view of the school of Goldstein, which is particularly influenced by *Gestalt* psychology. On the basis of general figure and background relationships, the following peculiarities were shown: (1) unprecise figure formation, (2) increased difficulty of comprehension of details, along with easier grasp of the complex, (3) lack of *Bewegungsmotive,* (4) rapid fatigue of a special kind, (5) increased difficulty of adaptation when there was not complete loss and (6) a general tendency to improve which was unspecific. Zucker's aim was to understand all these peculiarities on the basis of a common functional disturbance. For a deeper comprehension of the special interpretations it is necessary to read the paper itself.

MICHAELS, Boston.

CHOLESTEATOMA OF THE MIDDLE AND POSTERIOR CRANIAL FOSSAE. G. L. MONTGOMERY and D. I. C. FINLAYSON, Brain **57**:177 (June) 1934.

A girl, aged 19, whose clinical symptoms were suggestive of a lesion of the right side of the cerebellum was found to have a tumor which occupied both the middle and the posterior fossa on the right side. In the middle fossa the wall of the growth represented the structure of dermis and sebaceous glands ("dermoid" cyst). The wall of the portion in the posterior fossa corresponded to epidermis ("pial epidermoid"). This is against the view that intracranial "dermoids" and "epidermoids" are to be regarded as separate entities.

MICHAELS, Boston.

CEPHALIC DYSOSTOSIS. C. ALLEN, J. Neurol. & Psychopath. **14**:332 (April) 1934.

Allen describes a case of hypertelorism in a woman, aged 58, with amentia, epilepsy and a paranoid psychosis. This rare condition is characterized by excessive width between the eyes and a broad nasal bridge, with widely opened nasal passages, strabismus and prognathism. In this patient there were a marked scaphoid bone and a dolichocephalic head, with some exophthalmos and ptosis of the lids. Allen says that this is the first reported case with an associated psychosis. After a brief discussion of the various types of cephalic dysostoses and their etiology he suggests that their causation lies in failure of the growth of various portions of the brain on which the growth of the adjacent skull depends.

SPERLING, Philadelphia.

LATE AMAUROTIC IDIOCY OF THE VOGT-SPIELMEYER TYPE, WITH RETINITIS PIGMENTOSA: RELATIONS TO NIEMANN-PICK'S DISEASE. G. MARINESCO, Rev. d'oto-neuro-opht. **12**:39 (Jan.) 1934.

The problem of the intimate relationship of amaurotic idiocy with Tay-Sachs' and with Niemann-Pick's disease involves also the late forms in which the lesions affect the central nervous system, the parenchyma of other organs and the reticulo-endothelial apparatus. There is difference of opinion as to this relationship, but Kufs thought that one is not justified in denying it because the two

diseases do not always coincide. He also believed that involvement of the central nervous system depends less on the neuro-ectodermal origin than on the histochemical structure of its elements. Junius believed that there is a relationship between familial amaurotic idiocy, Niemann-Pick's disease and Gaucher's disease. In the case of Gaucher's disease reported by Lindau-Lund the histologic lesions of the neuraxis resembled those of amaurotic idiocy, and even the eyeground showed changes like those in Tay-Sachs' disease.

The case of a girl, aged 9 years, in which an autopsy was performed, is reported. The report of the autopsy is confined to a description of the retinal changes, which included especially profound alterations in the layer of rods and cones, disappearance of the internal granular layer and fatty degeneration of the nerve cells.

DENNIS, San Diego, Calif.

THE SYMPTOMATOLOGY OF TUMORS OF THE TEMPORAL LOBE. H. GANNER and G. STIEFLER, Arch. f. Psychiat. **101**:399 (Dec.) 1933.

Ganner and Stiefler report six cases of tumor of the temporal lobe, with clinical and pathologic studies. The patients consisted of four men and two women, and the age at onset ranged between 26 and 52 years. Three of the tumors were slow-growing astrocytomas, the duration of the illness being three and one-half, six and twelve years, respectively. The other three were: two glioblastomas, with a clinical course of two months' duration, and one medulloblastoma, with a duration of three months. Of the general symptoms of tumor of the brain, headache was present in all cases. In the three acute cases headache was the first symptom. In the others it developed later in the disease. Vertigo was also present in all cases and, like headache, was one of the first symptoms in the acute cases. Vomiting occurred in only two of the acute cases, whereas definite swelling of the disk was found in only one acute case. In two of the chronic cases a "beginning" swelling was described shortly before death. Psychic symptoms were noted in four cases. In some of these the symptoms were those of personality changes which developed slowly; in others, there were acute confusional states with hallucinations and incoherence. In two cases no positive roentgen findings could be demonstrated; in the others, various indications were obtained, such as flattening of the sella turcica, destruction of bone and signs of generally increased intracranial pressure. In two of the acute cases the visual fields could not be tested; in the others there was contralateral homonymous hemianopia, and in one case there was a concentric constriction of the visual field. Signs referable to the pyramidal tract and weakness of the side opposite to the tumor were present in all cases. In some, only the arm was affected; in others, both the arm and the leg. There was also weakness of the facial and other cranial nerves in some cases. Sensory disturbances were present in only one case in which a contralateral diminution of sensation was found. In one case there was a diminution in the sense of hearing on the same side as the tumor, and in the other cases there were no auditory disturbances. The sense of smell was disturbed in one case, in which there were also epileptiform convulsions with hallucinations of smell as an aura. Speech remained intact in only two cases. In two of the chronic cases there was difficulty in finding words, with paraphasia. In two of the acute cases there was paraphasia, in one associated with incoherence and in the other with sensory aphasia.

MALAMUD, Iowa City.

Diseases of the Spinal Cord

POLIOMYELITIS: A STUDY OF 410 PATIENTS AT THE PHILADELPHIA HOSPITAL FOR CONTAGIOUS DISEASES. PASCAL F. LUCCHESI, Am. J. M. Sc. **188**:515 (Oct.) 1934.

In 410 cases which were thought to be instances of poliomyelitis the diagnosis was confirmed in 304 (74.1 per cent). A statistical analysis of these cases is

presented from the point of view of age, sex, race, incidence of signs and symptoms, distribution of paralysis, serum treatment, paralysis and mortality. Two hundred and fifty-four patients (83.5 per cent) received serum; 124 of these showed evidence of weakness or paralysis on admission to the hospital; on discharge this number increased to 154. Fifty patients (16.5 per cent) received no serum on admission; 28 of these showed evidence of weakness or paralysis; on discharge this number increased to 38. It is concluded that convalescent serum was of little value in the prevention of paralysis.

MICHAELS, Boston.

FAMILIAL PERIODIC PARALYSIS AND ITS TRANSITION INTO SPINAL MUSCULAR ATROPHY. A. BIEMOND and A. POLAK DANIELS, Brain **57**:91 (June) 1934.

A description of the first Dutch family in which periodic paralysis appeared in three generations (fourteen cases) is given. In one of the cases chemical analyses were performed during an attack and during an interval; the results point to a shift in the sympathicotonic direction. The pathophysiology is suggestive of an important alteration of the chemistry of some of the striated muscles. Anatomic examination offers no help concerning the essential nature of the disease. There is a distinct type of spinal muscular atrophy which occurs in connection with familial periodic paralysis. By adopting the presence of two pathologic hereditary factors, both being dominant, the authors believe they have found a genetic explanation, according to Mendel's law, for this family.

MICHAELS, Boston.

THE MYOTONIA ACQUISITA IN RELATION TO THE POSTNEURITIC MUSCULAR HYPERTROPHIES. KNUD H. CRABBE, Brain **57**:184 (June) 1934.

Crabbe describes three cases in which true muscular hypertrophy (different from the pseudohypertrophy of the progressive myopathies) developed after an acute illness. In one case the hypertrophy was associated with myotonic symptoms; in the other two no myotonia was observed. If the muscle hypertrophies as a whole, no myotonia results; if the sarcoplasm especially hypertrophies a myotonic condition will be the consequence. In the thirty-four cases of myotonia acquisita reported in the literature all the patients were male and the age of onset (when given) was between 15 and 44 years. It is concluded that myotonia acquisita and true muscular hypertrophy are variations of the same abnormality: an abnormal regeneration after a neuritic process.

MICHAELS, Boston.

ACUTE EPIDURAL SPINAL ABSCESS. LEONARD ABRAHAMSON, A. A. MCCONNELL and G. R. WILSON, Brit. M. J. **1**:1114 (June 23) 1934.

A case of epidural spinal abscesses is presented in which a correct diagnosis and localization were made prior to a successful operation. The patient was a school girl, aged 14, whose first symptom was vague pain in the back. It gradually increased until it became so severe that it was relieved only little by drugs, including morphine. Pins and needles sensations in the legs appeared; spasm of the abdominal muscles occurred; the tendon reflexes became exaggerated in the lower extremities, and constipation was intense. The pulse rate and temperature were elevated, and on the eighth day a tentative diagnosis of epidural spinal abscess was made. By the following morning numbness and paralysis appeared in the legs. Retention of urine was noted, and the patient became restless and occasionally delirious. The temperature was 100.4 F.; the pulse rate, 130, and the respiratory rate, 32. Further progression of signs and symptoms, and particularly the girdle pain just below the umbilicus, suggested a lesion as high as the tenth dorsal segment of the cord. Anesthesia in the upper part of Scarpa's triangle suggested involvement of the second lumbar nerve root.

Except for the fact that the fluid was slightly yellow, spinal puncture was not of much diagnostic value. Iodized poppy-seed oil 40 per cent was injected by suboccipital puncture. Roentgenograms showed that the iodized oil was arrested at the eighth dorsal vertebra. The laminae of the eighth, ninth and tenth dorsal

vertebrae were removed. A pure culture of Staphylococcus aureus was grown from pus from the abscess.

About two months after the operation the patient could walk, though the gait was still spastic. Improvement continued, and at the end of nine months the patient was normal in every way.

Epidural spinal abscess may offer considerable difficulty in diagnosis, and many of the cases are either diagnosed too late or missed entirely. Pain is the earliest and the most important symptom. It is severe and persistent. In addition to being present in the back, it may radiate along the nerve trunks. Paralysis may come on within a few hours, but there is usually a latent period up to several days before motor symptoms appear. There may be stiffness and tenderness in the back and neck with pain on movement. With the appearance of paralysis, there is implication of the sphincters. Disturbance of sensation may appear and extend upward. General septic symptoms vary. Roentgenographic examination is helpful only when osteomyelitis has been present for some time. Lumbar puncture may show pus or evidence of compression. It may be followed by septic infection of the meninges. Roentgenography preceded by intracisternal introduction of iodized oil is indicated when neurologic localization is not adequate.

The mortality in untreated cases is 100 per cent. Of sixty cases collected by the authors from the literature, operation was performed in thirty. Twenty patients survived. In many cases recovery was incomplete.

FERGUSON, Niagara Falls, N. Y.

BROWN-SÉQUARD SYNDROME FOLLOWING MEDULLARY COMPRESSION DUE TO A PSEUDOTUMOR OF SYPHILITIC NATURE. ROQUES, SOREL, PLAQUES and PONS, Rev. neurol. **2**:667 (Nov.) 1934.

The patient, aged 49, complained of paralysis of the left lower limb, which had been present for one and one-half months. In addition to the paralysis there was severe unilateral pain, which resembled burning and torsion. The pains gradually disappeared, but there was increased weakness. There gradually developed impotence and disturbance of the bladder. The patient had been having crises of severe pains around the lower part of the chest for a considerable period. He had been in the hospital on previous occasions because of thoracic pain which had been considered pleural.

Physical examination showed good development and complete paralysis of the left lower limb. The patient was unable to stand because of extreme weakness in the right lower limb. Touch was preserved in this limb, but there was anesthesia for pain and temperature. Deep sensibility was fairly well preserved. The left lower limb showed integrity of all forms of sensation, except for an abolition of the deeper types. There was a sensory level at the ninth dorsal segment. This zone was continuous with an area of hypalgesia which extended completely around the trunk. The upper limbs and face were not involved. The reflexes were exaggerated in both lower limbs but were more active on the left, with clonus and a Babinski sign on that side. The abdominal reflexes were absent on the left. The vesical sphincter showed definite weakness. The Wassermann reaction of the blood was strongly positive. The Queckenstedt test showed complete block. The fluid was yellow and coagulated in fifteen seconds. A roentgenogram gave completely negative results. Antisyphilitic treatment was instituted, and within a short time the block was much less complete. Since treatment there has been a marked improvement in the neurologic signs, and the patient is able to walk comparatively normally.

WINKELMAN, Philadelphia.

EARLY INFANTILE PROGRESSIVE SPINAL MUSCULAR ATROPHY (WERDNIG-HOFFMANN) AND ITS RELATIONSHIP TO MYATONIA CONGENITA (OPPENHEIM). OTTO SCHILDKNECHT, Deutsche Ztschr. f. Nervenh. **134**:163 (July) 1934.

Many authorities consider progressive spinal muscular atrophy and myatonia congenita as one and the same disease; others, Bielschowsky among them, hold

them to be two distinct entities. Schildknecht reports five clinical cases and one with histologic observations with a view to throwing light on the subject. All five clinical cases were characterized by a typical constant progression of symptoms. Schildknecht considers this the most important diagnostic demarcation of Werdnig-Hoffmann's disease from a myatonia congenita. In three cases there was a hereditary history, a point which he considers of diagnostic importance in Werdnig-Hoffmann's disease, although the succeeding children born to the parents may be normal. From his own observations, Schildknecht is unable to substantiate the finding that the disease is first manifested in the second half of the first year of life. He observed symptoms as early as the third week. Fibrillary twitchings were present in four cases but were limited to the tongue. The electrical reactions were normal, or there was a partial reaction of degeneration.

In one case of Werdnig-Hoffmann's disease Schildknecht found regressive changes in the motor end-plates with gradual disappearance of the nerve elements. Comparing his findings with the anatomic changes observed in cases of Oppenheim's disease, he found certain similarities as well as some differences. In Oppenheim's disease the changes in the precentral convolution did not appear to be of a marked nature. Bielschowsky found the pyramidal cells to be smaller, with abnormal dendritic formation. In his case of Werdnig-Hoffmann's disease Schildknecht found marked diffuse changes in the ganglion cells. Neuronophagia was occasionally observed. The involvement of the cord was about the same in the two diseases. In neither were there inflammatory changes or circulatory disturbances.

The author found the peripheral nerves more markedly involved in Werdnig-Hoffmann's disease than in Oppenheim's disease. Schildknecht regards the change in the motor end-plates as a deciding factor in the differential diagnosis between the two. He found well developed end-plates as well as some which were badly damaged in a number of atrophic muscle fibers. This can be explained only on the basis that originally all the motor end-plates were well developed and that the regenerative changes took place some time later.

Schildknecht also noted morphologic differences between the two diseases. Bielschowsky found a splitting up of the finer terminal nerve branches, and the fibrillar net was entirely missing. Schildknecht found the end-plates well formed, and the nerve net showed all types of transition from normal to those containing only a few granules. He concludes that the changes in the end-plates begin in the center and spread to the periphery.

In Oppenheim's disease, therefore, the primary pathologic change is in the end-plates; in Werdnig-Hoffmann's disease the end-plates are primarily normal and only later undergo degeneration. This leads to the conclusion that the changes in the anterior horn cells of the cord differ in the two diseases, although anatomically the end process is the same. It is inconceivable that in Werdnig-Hoffmann's disease the cells could have been pathologic from the beginning. Under such conditions normal end-plates could not be developed. Likewise it cannot be assumed that in Oppenheim's disease the degeneration follows a normal condition.

The pyramidal cells in the precentral area in Werdnig-Hoffmann's disease are more severely involved than in myatonia congenita. The changes in the muscles in both diseases are secondary, as a result of the destruction of the peripheral motor neuron, and especially because of the incomplete contact between the muscle and the nervous system.

From his observations Schildknecht considers that Oppenheim's and Werdnig-Hoffmann's diseases are distinct entities. The difference in prognosis of the two conditions thus becomes intelligible. In Oppenheim's disease there is incomplete development, which is capable of restitution and clinical improvement. In Werdnig-Hoffmann's disease a degenerative alteration is the primary factor. Progression of the degeneration is expressed in progression of paralysis. It is evident also that in not all cases will myatonia show improvement.

BERNIS, Rochester, N. Y.

Treatment, Neurosurgery

ACUTE POLIOMYELITIS: THERAPY BY BLOOD TRANSFUSIONS FROM IMMUNE DONORS. IRVING SHERMAN, Am. J. Dis. Child. **47**:533 (March) 1934.

From a study of the effects of administering whole blood from convalescent donors to seventy-one children suffering from poliomyelitis, Sherman concludes that this form of therapy is the treatment of choice in acute cases of infantile paralysis. The work was done during the epidemic in Brooklyn in 1931, in which the general mortality rate was about 10 per cent and the incidence of paralysis 29 per cent. In a series of fifty-five patients treated with convalescent serum the paralysis and mortality rates were as high in the treated as in the untreated group. But the mortality rate of the group that received whole blood was only 2.8 per cent in the preparalytic cases and 11 per cent in the paralytic cases. The total mortality was only 7 per cent (or, if two patients who were moribund when the transfusions were started are excluded, only 4 per cent). The incidence of paralysis was less than 9 per cent, as compared with the general incidence of 29 per cent in untreated patients and 50 per cent in those treated with serum. The effect of the transfusion on the general symptoms, such as fever, headache, vomiting and prostration, was strikingly beneficial. From 150 to 400 cc. of blood was administered, and as a rule a single transfusion was adequate.

DAVIDSON, Newark, N. J.

THE EFFECT OF NON-SEDATIVE DRUGS AND OTHER MEASURES IN MIGRAINE WITH ESPECIAL REFERENCE TO ERGOTAMIN TARTRATE. SAMUEL BROCK, MARY O'SULLIVAN and DAVID YOUNG, Am. J. M. Sc. **188**:253 (Aug.) 1934.

Subcutaneous injections of various nonsedative drugs were administered to nineteen women and six men. No consistent provocative measure was found to induce headache. The gonadotropic principle of the urine of pregnant women, histamine and an estrogenic substance were sometimes successful. Hyperpnea also did not produce headache. The hypodermic injection of ergotamine tartrate resulted in the most striking benefit. Drugs, such as acetyl β-choline, amyl nitrite and histamine, which are supposed to induce vasodilatation did not invariably give relief. The injection of calcium preparations intravenously and the administration of ovarian follicular hormone were of no help. It is concluded that vasospasm is probably a secondary effect of, and not a primary factor in, migraine.

MICHAELS, Boston.

YEAST OR VITAMIN B_2 AS "EXTRINSIC FACTOR" IN TREATMENT OF PERNICIOUS ANEMIA. H. C. A. LASSEN and H. KRIEGER LASSEN, Am. J. M. Sc. **188**:461 (Oct.) 1934.

Eight patients with typical pernicious anemia were treated with various yeast preparations in order to ascertain the possible rôle of vitamin B_2 as an exogenous factor in the disease. The yeast preparations were assayed by tests on rats as to their content of vitamins B_1 and B_2. It is concluded that the extrinsic factor desired in the treatment for pernicious anemia is not identical with the B_2 factor of the vitamin B complex and, probably, not with any other fraction of this vitamin. Yeast appears either to be completely without any antianemic effect or possibly to contain minimal amounts of antianemic factor.

MICHAELS, Boston.

A SUCCESSFUL METHOD FOR VACCINATION AGAINST ACUTE ANTERIOR POLIOMYELITIS. JOHN A. KOLMER and ANNA M. RULE, Am. J. M. Sc. **188**:510 (Oct.) 1934.

Kolmer and Rule have successfully vaccinated seventeen monkeys by giving five injections of sodium ricinoleated vaccine in doses of 0.1 cc. per kilogram of body weight every five days. Subcutaneous injections of 0.05 cc. per kilogram of body

weight also produced effective immunity. In order for the vaccine to be effective it must contain some living but devitalized virus, which is accomplished by the sodium ricinoleate. The authors themselves received the vaccine by subcutaneous injection, and it was demonstrated that the vaccine was apparently capable of producing antibody for the poliomyelitis virus and probably sufficient for engendering immunity. It is believed that the administration of three subcutaneous injections of the vaccine at intervals of from five to seven days and in doses of from 0.05 to 0.1 cc. per kilogram of body weight is a safe and effective method for vaccination against acute anterior poliomyelitis.

MICHAELS, Boston.

THE RESULTS OF PHYSICAL AND MENTAL TRAINING ON MENTALLY DEFICIENT, BIRTH LESION CHILDREN. E. W. MARTZ and H. N. IRVINE, J. Juvenile Research **18**:42 (Jan.) 1934.

Martz and Irvine report the results of an experiment in training eighteen patients with birth palsies at Letchworth Village (Thiells, N. Y.); they ranged in age from 8 to 50 years and in intelligence quotient based on the Stanford-Binet test from 20 to 62. Physical training consisted of muscle reeducation along the lines suggested by Phelps at the Vineland Training School, together with certain especially devised manual tasks; mental training consisted of work in spelling, reading and arithmetic as well as other occupational instruction. Physical training had to be discontinued after a few months in the case of more than half the patients, either because of lack of cooperation or because age and great spasticity seemed to make the work unprofitable. It was continued for the full year during which the experiment was carried out in only two cases.

The six persons showing marked physical improvement were in the middle age range, the late teens or the early twenties, and included three persons with paraplegia, two with hemiplegia and one with diplegia. Mental improvement, as indicated by a rise in the intelligence quotient, occurred in all but one person, and the functional and social levels of the patients were clearly raised. There seemed to be no direct relation between mental and physical improvement.

McBRIDE, Philadelphia.

NARCOSIS AND MENTAL FUNCTION. J. H. QUASTEL, Psychiatric Quart. **8**:227 (April) 1934.

Deficiency of oxygen narcosis, alcoholism and certain psychopathic states are associated with a similar mental picture—early euphoria, confusion, loss of insight and dulness. Quastel's experiments show that narcotic drugs inhibit the oxidation of dextrose and lactic acid—two products the breakdown of which is a characteristic feature of respiration of the nervous system. The products of the breakdown of tyrosine and tryptophan (such as indole and tyramine), which are normally detoxicated by the liver, depress the oxidation of lactic acid and dextrose just as narcotics and anoxemia do. The author suggests that if, because of breakdown or overproduction of these products, an excess of indole, tyramine and similar substances appears, the metabolism of the nervous system will be affected adversely, precisely as if the patient were undergoing alcoholism, anoxemia or narcosis. This, he believes, is the physiologic basis underlying many psychoses.

The value of narcosis in the treatment of mental disease is well known, but the toxic effects of the narcosis have discouraged its full usage. These untoward results are associated with the development of ketonuria. Quastel reports that the joint administration of insulin and dextrose has prevented the appearance of ketonuria and other unfavorable complications and has rendered the narcosis safe. Good results have been obtained in cases of early schizophrenia, of neuroses and of manic-depressive psychosis. Apparently, during the prolonged period of narcosis the metabolites or other toxic substances are eliminated, while the low level of activity prevents their reformation in excess.

DAVIDSON, Newark, N. J.

HYPERTONIC RECTAL SALINE FOR INTRACRANIAL INJURY IN THE NEWBORN. ALAN MONCRIEFF, Brit. M. J. **1**:1068 (June 16) 1934.

Moncrieff cites the work of Cruickshank, who expressed the belief that increased intracranial pressure is a factor of great importance as a cause of death of the newborn. Hemorrhage into the substance of the brain itself occurs only in unusual circumstances. Increased intracranial pressure may occur when labor has been unusually difficult, with a prolonged second stage, occipitoposterior presentations, forceps deliveries and other departures from normal. Premature babies are particularly liable to intracranial injuries. Respiratory difficulties may be present from the onset, but more usually the symptoms have developed gradually in the first two or three days of life. A refusal to eat, with deepening somnolence, often alternating with periods of restlessness and crying, is usually the first manifestation. Recurrent vomiting may occur, the fontanel bulges, and frequent twitchings of the facial muscles and limbs are observed. Failure of respiration with attacks of cyanosis are a constant feature.

The present method of the introduction of injections of hypertonic saline solution rectally has been evolved over a period of nearly twelve months. It has been used in about twenty cases. From 2 to 3 ounces of 10 per cent saline solution is introduced into the rectum of the new-born babe as soon as the symptoms appear. This must be done slowly, and the buttocks must be held together to insure retention as long as possible. The injections can be repeated at intervals of four hours or longer. The method is wholly free from harm. One-half grain (0.032 Gm.) of chloral may be given if restlessness or twitching is present. Five per cent carbon dioxide in oxygen is of great value for failure of respiration. When hemorrhage is suspected, as indicated by the rapid onset of symptoms shortly after delivery, 10 cc. of the mother's blood is injected intramuscularly into the baby. It is not maintained that hypertonic saline solution administered rectally can accomplish anything in cases in which meningeal or cerebral hemorrhage has occurred. The results have been so encouraging in cases of increased intracranial pressure that this treatment is used prophylactically in cases in which delivery has been difficult.

FERGUSON, Niagara Falls, N. Y.

THE TREATMENT OF TOXICOMANIA BY VEGETABLE LIPOIDS. ROGER DUPONY and MAURICE DELAVILLE, Encéphale **29**:145 (March) 1934.

In the main this article is concerned with the treatment of persons addicted to the use of morphine. The well known work of Overton showing a differential solubility in water and in lipoids of certain narcotic substances (alcohol, nicotine, ether, morphine, cocaine, etc.) is used as the basis. Owing to this double solubility, an invasion of the living cell with the phenomena of narcosis resulting is possible. The treatment here outlined is a "lipoidal" one, i. e., neutralization of the antigenic substances developed in the organism by vegetable lipoids in the form of a sterile colloidal form. The treatment consists of a series of injections of oily substances (olive oil, lecithin and insulin) in conjunction with accessory preparations designed to insure elimination of toxins, sedative action on the nervous system, maintenance of general body tone, etc. Such treatment, in résumé, is as follows: Between 7 and 8 o'clock, laxative pills, from 10 to 15 drops of phenobarbital, 30 Gm. of syrup, an ampule of vegetable lipoid and ephedrine; at 10 a. m., 2 cc. of sparteine in camphor in oil hypodermically; at 11 a. m., 1 ampule of lipoid, ephedrine, and if necessary an injection of solution of posterior pituitary and epinephrine hydrochloride at 3 p. m., 30 Gm. of syrup and vegetable lipoid; at 5 p. m., sparteine in camphor in oil; at 6 p. m., vegetable lipoid, and again, if necessary, an injection of solution of posterior pituitary and epinephrine; at 9 and at 10 p. m., vegetable lipoid and from 20 to 30 drops of phenobarbital. During the night, if necessary, a sedative is given (butylethyl barbituric acid). In general, this routine is continued for four or five days, with rapid withdrawal of the drug to which the patient is addicted. Thirty cases are outlined in which good results were obtained.

ANDERSON, Los Angeles.

URGENT TREATMENT OF ACUTE RETROBULBAR OPTIC NEURITIS OF SINUS ORIGIN: PHENOLIZATION. M. TERRACOL, Rev. d'oto-neuro-opht. **12**:401 (June) 1934.

Terracol reviews the subject of the treatment of acute retrobulbar optic neuritis and states that the confusion existing is due to the following factors: 1. Ocular disturbances are in the domain of pure ophthalmology, and yet they have been the subject of discussion by rhinologists. 2. The definite formula that retrobulbar optic neuritis is always due to infection in the sinuses and requires intervention on the sphenoid sinuses has been imposed. 3. The term retrobulbar optic neuritis was introduced by von Graefe to designate lesions more highly situated in the optic nerve than those which cause peripheral paralyses. Ophthalmologists themselves argue over the pathogenic and symptomatic substratum of retrobulbar optic neuritis.

The present tendency is no longer to regard neuritis as a special malady but under this term to include all diseases of the posterior segment of the optic nerve (between the chiasm and the point of penetration of the central vessels of the retina). Histologic studies do not show that the nerve structure is altered by the penetration of the retinal vessels. Hence, this subdivision of the nerve has only a topographic value. Not all patients with retrobulbar optic neuritis recover spontaneously, and in about 50 per cent of the cases the etiology is not discovered.

In collaboration with Canuyt, Terracol has conducted researches on retrobulbar neuritis for several years. The conclusions are that an infection of the posterior sinuses or the bacterial toxins can easily reach the optic nerve; the causal factors may be arranged in the following order: syphilis, infectious rhinosinusitis, disseminated sclerosis, heredity, intoxications and vasomotor disturbances. Syphilis is too often forgotten; but, on the other hand, systematic treatment in the face of the lack of all signs of syphilis is a fault, because each day the lesion progresses. Sinusitis does not always mean the formation of pus; there are various grades of inflammation. The sinusitis etiology ought not to be disregarded, and intervention must often be early; all patients with optic neuritis should have a thorough rhinologic examination. Per contra, sinusitis alone as an etiologic factor must not be assumed. It is the duty of the rhinologist to furnish the ophthalmologist with as precise data as possible on the state of the sinuses. Special methods of examination are required: shrinking of the region with cocaine and epinephrine, catheterization and puncture of the sinuses and roentgenograms. The ophthalmologist must direct the treatment and determine the indications for operation. Trepanation of the sphenoid sinus is the most logical procedure, but it should be reserved for serious cases. When the condition is unilateral and evolves slowly, with signs often atypical, excellent results are obtained by phenolization. Under close control by the oculist, if the disease is not ameliorated, immediate operation on the sinuses is indicated.

DENNIS, San Diego, Calif.

AIR INFLATION BY THE LUMBAR ROUTE AS A THERAPEUTIC MEASURE IN EPILEPSY. RUDOLF FRIEDMANN and J. SCHEINKER, Deutsche Ztschr. f. Nervenh. **133**:35 (Nov.) 1933.

Friedmann and Scheinker investigated the therapeutic possibilities of the inflation of air introduced by the lumbar route in cases of epilepsy. Half an hour after an injection of a mixture of the hydrochlorides of the opium alkaloids, scopolamine and caffeine (in children ether anesthesia was used), the first 10 cc. of fluid withdrawn was replaced by inflation of 5 cc. of air, and this deficiency of 5 cc. was maintained until from 50 to 60 cc. of fluid was withdrawn. When larger quantities of fluid were withdrawn the difference was increased to 10 or 15 cc. The quantity of fluid removed varied from 50 to 100 cc. The authors found from 40 to 50 cc. to be the minimal quantity requisite for encephalographic as well as for therapeutic purposes. The procedure is best accomplished with the patient in a sitting position.

Frontal headaches usually appear when from 30 to 40 cc. of fluid has been withdrawn and replaced by air. Likewise nausea and vomiting may set in. Girdle

pressure pain, more often in the area of the neck, is often produced. There are noticeable pallor of the face and a slowing or acceleration of the pulse with arrhythmia. Epileptic attacks during inflation were seldom observed. The age of the patient offers no objection to this procedure. Young children stand air inflation even better than older persons. Nor do severe epileptic attacks offer a contraindication as long as the general condition of the patient is satisfactory. Medication is to be continued or partly modified after the inflation.

Forty-three cases are reported, twenty-eight in women and fifteen in men; in twenty-six the diagnosis was genuine epilepsy, in five late epilepsy, in ten symptomatic epilepsy and in two traumatic epilepsy. The observation covered a period of four years. The authors consider as instances of genuine epilepsy those cases in which the epileptic attacks began in early childhood with no observable neurologic pathologic process and with no history of injury to the head or of a previous inflammatory condition of the brain. Some of the patients suffered mild and repeated attacks; others were subject to more severe attacks, and some suffered from mixed types.

The twenty-six patients with conditions diagnosed as genuine epilepsy received a total of thirty-six inflations of air. The authors report good results in seven patients, partial improvement in ten and no improvement in fifteen. The patients reported as showing good results remained free from attacks for from two weeks to eight months. Following inflation with air the patients continued to receive medication in full or diminished doses. The improvement became manifest not only in relief from attacks, but the psychic response also became more normal. There was also considerable relief from the headaches. The patients were less torpid, less irritable and less depressed; they became more lively and more talkative, took more interest in the surroundings and showed improvement of memory. Under partial improvement, the authors include diminution in the severity and frequency of the attacks. There were ten cases in this group; improvement in the mental and physical condition of the patients also occurred. Especially was there marked improvement in the attacks of headaches.

Fifteen patients remained uninfluenced by the inflation of air. The largest number of this group also remained uninfluenced by any form of medication.

With reference to the quantity of air requisite for obtaining a good roentgenogram, the minimum was 40 cc. A larger quantity is desirable. When possible inflation should be done at least twice; but even with the best technic the encephalographic picture may differ with each inflation. Friedmann and Scheinker have seen encephalograms displaying a pathologic picture in cases of genuine epilepsy, and therefore they cannot agree with the opinion expressed by some that in cases of genuine epilepsy there is always a normal encephalogram and that such a finding is prerequisite for this diagnosis. As for the relationship between the encephalographic picture and the therapeutic results with air inflation, the authors found that a normal encephalogram was obtained in six of the seven cases in which the results were considered good. In one the air did not appear to have entered the cranium until a considerable time after the inflation. In one case a normal encephalogram was obtained after the first inflation, and the patient remained free from attacks for six months; then after the second inflation the encephalogram showed pathologic changes. Of the ten cases in which partial improvement was reported, a normal encephalogram was found in eight. This indicates that anatomic integrity of the spinal fluid spaces is prerequisite for successful treatment with air inflation. Among the fifteen in which treatment was not successful, pathologic changes were found in the encephalograms in eight cases. On comparison of roentgenograms of the head with encephalograms of the same patients, in twenty-two cases of genuine epilepsy the authors found normal roentgenograms in twelve cases; in seven the picture was on the borderline, and in three it showed outspokenly pathologic changes.

In the group of five cases of late epilepsy even better results were secured. Only one person failed to show any response; the other four remained free from attacks for from five weeks to five months. In four cases in this group a normal

roentgenogram of the head was obtained twice; in one the picture was on the borderline and in another no roentgenogram was taken. Of the encephalograms, two were normal, and one showed pathologic changes, and in one case an encephalogram was not made. In one case a glioma was subsequently found.

Of the group of cases classed as instances of symptomatic epilepsy, six were cases of residual infantile paralysis, one of syphilitic meningitis, one of microcephalic imbecility and one of hydrocephalus with hemiplegia, and in one a diagnosis was not made. Seventeen inflations were done. Five times the inflation was successful, six times unsuccessful and five times partially successful.

Of the two patients with traumatic epilepsy, one showed some improvement. This patient subsequently became entirely free from attacks after passing through a long infectious illness which was accompanied by high fever. The second patient, a girl aged 18, after a head injury had jacksonian attacks of motor and sensory character. These were relieved by medication and roentgen treatment. After a second injury to the head the attacks recurred. She then failed to respond to the same mode of treatment. Inflation gave relief from the motor attacks; the sensory attacks remained unaffected.

The forty-three patients received a total of sixty inflations. Of this number six could not be utilized; good results were obtained from fifteen and partially good results from seventeen, and twenty-two were complete failures. The authors have found that epileptic patients tolerate air inflation as well as other patients. They are of the opinion that the good results obtained in cases of genuine epilepsy and in some cases of late epilepsy are due probably to the freeing of meningeal adhesions, thus permitting a free circulation of fluid. The carrying off of toxic substances may also play a rôle. However, they are not certain that the same holds true with reference to the other two types of epilepsy, since in these pathologic changes are present, although the presence of pathologic changes in the encephalogram in these cases does not exclude the possible presence of disturbed fluid circulation. In agreement with others, the authors found that epilepsy following infantile cerebral paralysis is favorably influenced by air inflation, especially during childhood. Repeated injections of air in persons with epilepsy are not followed by ill effects.

BERNIS, Rochester, N. Y.

Society Transactions

NEUROLOGICAL SOCIETY OF PARIS

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M. VURPAS, *President*

Revue Neurologique **1**:809, 1934. Abstracted by WALTER FREEMAN, M.D., Washington, D. C.

THE VEGETATIVE CENTERS OF THE MEDIAN DIENCEPHALON. ANATOMIC STUDY. L. LARUELLE.

There are vegetative centers in the cerebral cortex, the diencephalon, the brain stem and the spinal cord. The median and lateral portions of the center in the diencephalon are not well known. The median portion comprises the walls of the third ventricle. The lateral portion consists of the supra-optic ganglia. There are many nuclear masses located here, but it appears that in the rising scale of animal life there is a reduction rather than an increase in the nuclear complexity. However, the problem is rather complicated by the occurrence of nuclei of mixed character, somatic and vegetative, and by the widespread occurrence of cells of the structural characteristics of the central gray matter.

This study has been confined to the vegetative centers located in the median portion of the diencephalon. Study of this part of the brain is difficult on account of cellular peculiarities, the tenuity of the cellular elements and the somewhat inaccurate methods at present available. However, for differentiation of the nuclear masses four criteria are available: *(a)* histologic structure of the cellular type; *(b)* intimate structure of the nuclei; *(c)* topographic characteristics of the cellular groups, and *(d)* connections of each nucleus. The Nissl technic is of value, but of all the silver stains that of Reumont is the most satisfactory because it impregnates every cellular element and can be used in serial sections. The plane of section is important because vegetative cells tend to be of a rather elongated bipolar type and this will be missed if the sections are cut transversely; moreover, the arrangement of cells in relation to one another is characteristically the closely packed group parallel with the stream of fibers and resembling a school of fish. The vegetative type of cell has a large nucleus, a dusty chromatin substance and a clear paranuclear zone and not infrequently contains some lipoid material.

The various nuclei of the median portion of the diencephalon in man are considered to be ten in number: (1) the grisea centralis; (2) the nucleus supra-opticus; (3) the nucleus paraventricularis; (4) the nucleus laterobasalis tuberis; (5) the nucleus mamillo-infundibularis or tuberomamillaris for which the name nucleus tuberomamillo-trigonalis is suggested; (6) the nuclei corporis mamillaris, comprising the large cell nucleus, the small cell nucleus and the posterolateral gray nucleus of Greving; (7) the nucleus intercalatus; (8) the nucleus substantiae reticularis hypothalamicae; (9) the nucleus reuniens, and (10) the nucleus paramedialis. Greving has described the following additional nuclei: (11) the nucleus pallido-infundibularis; (12) the nucleus interfornicatus, and (13) the corpus subthalamicum of Luys. Laruelle, however, considers these to be either parts of previously classified nuclei or not connected with the vegetative system. At the end of his work there is a nine column table showing the various terminology designating the nuclei of the median portion of the diencephalon.

There follows a rather detailed description of these various centers with excellent and appropriate photomicrographs.

Laruelle states that he does not attempt to describe the conduction pathways in the hypothalamus, which are complex. The somatic pathways comprise those which connect the various primary, secondary and tertiary centers of the rhinencephalic system. The somatovegetative pathways are likewise represented by rhinencephalic fibers, but these end in the nuclei of the median part of the diencephalon. A number of other fibers connect the mamillary body with the olfactory cortex; these are represented in the hypothalamus by the anterior pillars of the fornix. Another rather scanty group penetrating the walls of the tuber cinereum represents the connection between the corpus striatum and the hypothalamus. The purely vegetative fibers are composed largely of those connecting the hypothalamic nuclei with each other and with the hypophysis. Greving has designated these pathways as the tractus supra-opticohypophysealis and the tractus paraventriculocinereus. There are partly crossing fibers among these tracts; thus, a rich nerve supply to the hypophysis is established. Moreover, there is a tangential paraventricular system, the fibers of which ramify beneath the ependymal cells and reveal end-plates either between or actually within the ependymal membrane.

It can be said in general that afferent pathways bring more or less elaborated olfactory impressions to the different centers of the median part of the diencephalon and that the efferent pathways are grouped into two systems, one acting directly on the hypophysis and the other, on a visceromotor or glandulo-effector nucleus, the "dorso-vagal nucleus." In many instances, however, though the connections can be established, the direction of the neural current can only be imagined.

The innervation of the hypophysis is complex, and the relation of this gland to the hormones is not completely understood. There is apparently direct transportation of the glandular hormones to the hypothalamus. The four systems of neural connections, namely, the tractus supra-opticohypophysealis, the tractus paraventriculohypophysealis, the tractus tuberobasalohypophysealis and a number of fibers emanating from the grisea centralis are reenforced by sympathetic filaments from the carotid plexus; most of these terminate in the posterior lobe; some terminate in the pars intermedia, and in view of the decussations one may gather that the two halves of the gland are in relation with each half of the hypothalamus, thus constituting a vegetative coupling with reversible action. Moreover, one may consider the hypophysis as activated by the keyboard of the hypothalamic nuclei, with each key giving a particular "sound," a special innervation. Certainly the functional multiplicity of the hormones of this gland is not found in its histologic structure.

Localization within the hypothalamus awaits further cytomyelino-architectural studies, as well as extirpation and stimulation experiments. The early opinion of Karplus and Kreidl that the corpus subthalamicum of Luys was responsible for the vegetative phenomena obtained by stimulation of the hypothalamus has been completely upset by more recent studies that have shown not only that the corpus Luysi is decidedly a motor ganglion but that similar physiologic effects are obtained on stimulation of other portions of the hypothalamus.

The architecture of the hypothalamus becomes simpler as one ascends the vertebrate scale, a decidedly strange fact, since the complexity of human life would seem to be greater than that of the lower animals. There are thirty nuclei in the rodent, fifteen in the dog and nine in man; moreover, the central gray matter of man differs even from that of the higher apes by the absence of small cells and the disappearance of the nucleus pedimenti lateralis. Whether this simplification is accompanied by telencephalization with greater dominance of the cerebral cortex cannot be stated owing to the present relatively meager knowledge of the vegetative centers in the cerebral cortex. The central gray matter is probably among the most important of all the elements of the median portion of the diencephalon. As the ventricular ependyma is not only a secreting surface but also a sensitive receptive surface, it is logical to consider the central gray matter as a center of elaboration and propagation for stimuli received at the level of this "internal surface" of the brain. The anatomic foundation is obviously seen in the end-

organs lying between or actually within the ependymal cells and is also indicated by the extreme sensitiveness to stimuli of various types. Furthermore, the efferent system arising in this location assures the play of vegetative reflexes carried out particularly by the parasympathetic system. The mamillary bodies seem to carry out both somatic and vegetative functions connected with olfactory impressions, the great importance of odors in the preservation of self and of species being recognized. The large cells of the substantia reticularis on either side of the foramen of Monro are presumably concerned with the function of sleep.

DISCUSSION (ABSTRACT)

J. NICOLESCO: Nicolesco discussed the new classification of the hypothalamic nuclei on the basis of his own work.

MAURICE DIDE: Dide discussed the cytologic types in the vegetative centers in the median diencephalon, pointing out some examples of amitotic division.

G. ROUSSY and MOSINGER: Roussy and Mosinger summarized their work on the anatomy and physiology of the hypothalamus with the aid of numerous photomicrographs and diagrams and emphasized the following points:

The vegetative system develops between the motor and the sensory portion of the neural tube; the hypothalamus is divided into an anterior and a posterior portion, the former being concerned largely with hypophyseal innervation and impregnated with hypophyseal colloid (a neurocrine process). The posterior portion of the hypothalamus, while connected with the anterior portion, is not influenced so directly and seems to be connected more with the mamillary structure. There follows a detailed study of the hypothalamic nuclei, differing in some features from that of Laruelle.

They emphasize particularly the occurrence of colloid and of secretory granules and lipoid substances in the cytoplasm of the cells and the fibrillary connections of one part with another.

Histophysiologic study of the vegetative function of the hypothalamus indicates secretory functions of the tangential, paraventricular and other nuclei in view of the clear paranuclear zone, intracytoplasmic vacuoles and fatty inclusions; osmic acid stains some of these cells dark and some light, apparently indicating two successive stages. Moreover, the intracytoplasmic granules are found in the external segments of the hypothalamomamillary nucleus, where the neurocrine process (absorption of hypophyseal colloid by the cells) is scarcely likely to occur. Discharge of the secretion may take place by the endoneural root or by the ventricular root, and it is interesting to note that the ependyma over the posterior paraventricular nucleus shows tubuliform invaginations.

Anatomically the thalamus appears to be endowed with the capacity of selecting stimuli transmitted to the hypothalamus, and thus the thalamus is brought into indirect relationship with the whole sensory, and also with the motor, nervous system. Moreover, all the endocrine glands can stimulate the hypothalamus through the general circulation; also it appears certain that the hypophyseohypothalamic neurocrine process is under the influence of the vegetative nervous system, since an exaggeration of the neurocrine process follows resection of the cervical portion of the sympathetic chains and the vagus nerve in dogs. Pathologic lesions in the vicinity of the hypothalamus can bring about evidence of disturbance of secretion; thus a meningioma of the lesser wing of the sphenoid bone or even simple hydrocephalus may give rise to acromegaly, and other syndromes may occur from simple pressure. Finally, the hypothalamus, like all parts of the vegetative nervous system, acts on the cortex not only by way of the hypothalamocortical pathways but also by way of the blood stream carrying hormones from various other glands. In effect, the cerebrospinal system, and with it the cortex, can be considered in relation to the vegetative system as an executive organ on the same level as a glandular one. The injection of epinephrine hydrochloride into the third ventricle produces shortening of motor and sensory chronaxia, while the subcutaneous injection of the drug lengthens the chronaxia.

THE APPROACH TO NEUROPHYSIOLOGIC ORIENTATION. AUGUSTE TOURNAY.

Free living animals require more or less homeostasis, as first indicated by Claude Bernard. This doctrine has been approached by Lavoisier, Flourens and Magendie and has since been greatly extended by Graham Brown, Gaskell, Hess and especially Karplus and Kreidl. The peripheral mechanism of homeostasis has been explained best by Cannon. Only two examples will be drawn at present, the need for oxygen and the need for water.

A. *Need for Oxygen.*—Many experiments have shown that there are centers controlling respiration; the simple classification of Lumsden reduces the respiratory process to an ingenious physiologic clockwork mechanism. By means of the technic of the "isolated head" and by means of the oscillograph, the rhythmic activities of the respiratory centers have been studied. The tension of carbon dioxide is the most important influence, but the concentration of hydrogen ions and the oxygen tension also influence the activity of the center. Respiration thus lends itself in a supple fashion to all these external circumstances.

There are, however, other correlations in homothermal animals. Respiration permits a loss of water in certain animals, thereby maintaining thermal equilibrium. The dog, for instance, when manifesting so-called heat dyspnea, does not exhibit respiratory embarrassment. Magne has shown that reflex polypnea is controlled by the vagus nerves. Respiratory changes are noted during operations on the hypothalamus, there being inhibition of respiration on stimulation of the most rostral portion of the thalamus, whereas stimulation about the fornix produces marked acceleration of the respiratory rate. Separation of the thalamus from the hypothalamus is likely to cause typical polypnea, and this reaction seems to be connected with the loss of heat. Tournay states that observations regarding respiratory function, thermal variations and loss of water are desirable.

B. *Need for Water.*—When the neurosurgeon in exploring the third ventricle in the conscious patient comes to the neighborhood of the infundibulum and asks the patient how he feels, the patient sometimes replies, "I feel well, but I am terribly thirsty." As a result of an analogous operative procedure the patient may manifest a desire to sleep. This center, therefore, seems to be a gage determining when the body is about ready to need water, as a gage would determine how soon a mill was about to run out of grist. Water enters and leaves the body in the liquid or gaseous state, but in the body it is bound more or less closely into various molecules, keeping the colloids and crystalloids in solution, maintaining the osmotic pressure and bathing the walls of organs. It seems, likewise, that there is a mobile mass of free liquid ready to replace at any time any apparent deficit. The question at issue is to determine what part the nervous system plays in this transport or interchange of fluid. At the incoming end, for instance, the intestinal villi act like little pumps and are obviously under the control of the plexus of Meissner. In the discharge of water, particularly in some lower animals, the lungs are of great importance. Excretion of water through the skin is an integral part of thermal regulation. It has been found experimentally that the water vapor content of expired air can vary independently of the ventilation, as though there were present an actual pulmonary sweating; for instance, when an animal is heated or chilled the amount of water vapor excreted in the expired air increases rapidly when the temperature reaches a certain level. Moreover, if the animal is chilled suddenly, there is a latent period before the water vapor content of the expired air returns to normal. These observations indicate that the changes are controlled by the vegetative nervous system. Moreover, if an animal is subjected successively to hot and cold baths the fluidity of the blood varies according to the temperature reached. Should the bounds be overstepped and too great heat applied, concentration instead of dilution is the result. In most instances it seems that the concentration of the blood is the prime factor in regulating the excretion of water. The phenomenon of thirst, according to Mayer, results from a permanent excitation of the nervous system caused by the circulating blood. There is little doubt, moreover, that the hypothalamus plays a predominant rôle in all this particular function, although there is no particular cellular group that can be looked on as the "thirst center."

Neurohumoral correlations represent the last and the most difficult phase of study presented by the vegetative system. These correlations control respiratory and thermal functions as well as sympathetic and vagus function and, moreover, by controlled experiments on transfer or cross-circulation, effects of the stimulation can be reproduced in a second animal. This indicates that there is liberated in the blood stream some substance, the sympathin of Elliott or the *Vagusstoff* of Loewi or substances that seem to bear a relationship, respectively, to epinephrine and acetylcholine. Moreover, the regulation of the balance between heat and cold. sleep and waking and anabolism and catabolism and the rhythmic exercise of these functions seem to be largely conditioned by the activity of the hypothalamus. Even in disease certain of these functions are carried out normally; others are carried on on a different plane of activity, for instance, during periods of high fever. What Claude Bernard spoke of as "the most sensitive of balances" and what Cannon referred to as homeostasis may well be the prime function of the hypothalamus.

DISCUSSION

J. NICOLESCO: The circulatory regulation appears to have some relationship with the cellular respiration, nutrition and the specific physiologic condition of the superior vegetative centers. The sensations experienced by patients during surgical intervention on the tuberohypophyseal region may result from changes in the pressure of the cerebrospinal fluid or from alteration in the speed of the circulation. The cells lining the floor of the third ventricle, which are flattened in certain parts adjacent to the infundibulum, seem to be particularly sensitive to these modifications.

EXPERIMENTS ON THE INFUNDIBULUM IN RELATION TO SLEEP. NERI, BORGATTI, BATNINI and SCATLIETTI.

The experiments were carried out on animals by means of cross-circulation. Blood was passed from the carotid artery of the donor on to the jugular vein of the recipient and returned from the femoral artery of the recipient to the femoral vein of the donor. Then, under roentgen control, a needle was driven into the region of the infundibulum of the donor. When the infundibulum was reached there were sudden slowing of the respiratory rhythm and increase in the blood pressure, and the dog fell asleep. None of these phenomena were observed in the animal receiving blood from the stimulated animal; hence it appeared that there is no likelihood of a hormonal or vasomotor mechanism in the conduction of sleep but rather that the reaction is a true nervous phenomenon.

DISCUSSION

J. LHERMITTE: The facts just reported are of great importance and agree well with clinical phenomena. As I have indicated in my work on sleep, an inhibition emanating from the diencephalomesencephalic region seems to exist during sleep. During the first part of sleep there is often an exaggeration of the spontaneous movements of the paralyzed lower limbs in subjects who have undergone section of the spinal cord.

NEW CLINICAL DATA ON THE METABOLISM OF WATER. C. RIZZO.

During the past twenty years the absolute predominance of the hypothalamus in the regulation of water balance has become accepted. The center is evidently sensitive to the concentration of blood, and in the normal person great diuresis results from the ingestion of a large quantity of fluid. This is the basis of the dilution tests first described by Kövesi and Volhard. Seventy per cent of persons respond with an immediate diuresis, but in 30 per cent there is more or less retention of fluid in the tissues or an exaggeration of the output of water by the kidneys. On the other hand, the output of chloride remains relatively constant in all persons. In certain persons the ingestion of massive amounts of water, from 7 to 8 liters,

gives rise to two successive maxima in output. The first is poor in chlorides and seems to be preponderantly an elimination of water; the second is richer in chlorides. The question is tied up with diabetes insipidus, but no definite relationships are yet established.

CLINICOPATHOLOGIC SYNDROMES DEPENDENT ON THE HYPOTHALAMIC VEGETATIVE APPARATUS. J. LHERMITTE.

If the mesodiencephalic vegetative centers influence the pituitary gland and are influenced by this secretion, the same centers act also on the other endocrine glands, and their own function is modified by the activities of the glands themselves. According to most authors, it is impossible to dissociate the local symptoms referable to the vegetative nervous system from signs of involvement of the pituitary gland. Lhermitte, however, states that it is important not to confuse physiopathologic clinical and anatomopathologic manifestations. According to Trocello, some of the myelinated fibers running to the hypophysis are sensory, because the gland has no muscular fibers. This is also indicated by the pain experienced when the hypophysis is touched. Collin has found some Vater-Pacini corpuscles in the tentorium sellae, and this proves that the tissue covering the gland is sensitive to distention. The pituitary gland and the hypothalamus are linked not only by nerve fibers but also by special vascular systems described by Gregor, Poppa and Fielding. The blood from the gland is carried by small vessels to the diencephalon. The hypothalamic perikaryons bring about a more or less rigorous control of hypophyseal function. Moreover, the pituitary gland influences the diencephalic nuclei by its secretion. The colloidal substance of the hypophysis influences the nervous system not only by way of the general blood stream but also by that of the portal stream and directly through the spaces in the nerve tissue (a neurocrine process) and finally by the ventricular cavities (a hydrencephalocrine process). Moreover, there is actual secretion on the part of the nerve cells themselves in this region, indicated by the presence of granules, globules and hyaloid spaces in the cytoplasm of the cells. According to the belief of some authors, the hypothalamus may be regarded as being endowed with a double activity: neural and hormonal.

The same conclusions were reached by physiologic studies showing that extracts of the tissues contained substances having oxytocic, hypertensive, melanophore-dilator and antidiuretic substances identical with those of hypophyseal extracts. Moreover, the abdominal implantation of the tuber in the guinea-pig has given rise to the phenomena of inhibition and excitation. Cushing has shown (1) that the ventricular fluid contains a substance the properties of which are identical with those of extracts of the neurohypophysis and (2) that injection of solution of posterior pituitary into the infundibulum produces intense parasympathetic excitation, just as the injection of pilocarpine hydrochloride does. If the infundibulotuberal region is destroyed by an infiltrating glioma the effect is not obtained. With these things in mind one may consider the following interactions of the hypophysis and the diencephalon: 1. A lesion limited to the hypophysis annihilating the neurocrine, hematoneurocrine and hydrencephalocrine processes suppresses the excitation normally produced by the hypophyseal or diencephalic secretion. 2. An alteration of the hypothalamic diencephalon, by destroying the zone of the infundibulum sensitive to hormones, leads to a serious disturbance in the function of the vegetative system. 3. The suppression of permeability of the infundibulum by a morbid process renders the hydrencephalocrine process impossible and therefore annihilates the whole series of normal vegetative stimuli. 4. The conjoint destruction of the pituitary gland and the hypothalamus puts out of function both the hormonal and the nervous regulation.

1. *Syndromes of Hypophyseal Origin.*—Today it is no longer doubted that acromegaly, gigantism, dwarfism and pituitary basophilism are referable to the hypophysis itself. Regarding "hypophyseal cachexia" or Simmonds' disease there is less accord. Experimentally it has been shown that the complete destruction of the pituitary gland does not bring about death or cachexia in the animal, and in

some clinical cases of Simmonds' disease the condition appears to be secondary to some destruction of the pituitary gland or to alterations in the infundibulum.

2. *Infundibulotuberal Syndromes.*—(*a*) Diabetes Insipidus: A lesion limited to the hypophysis does not cause this syndrome. The fact that an extract of the posterior lobe of the pituitary gland depresses the diuretic function cannot be denied, but that does not prove that the pathologic changes in the posterior lobe of the pituitary gland are the cause of the syndrome any more than the fact that insulin controls glycosuria proves that diabetes is caused by degeneration of the islets of the pancreas. Moreover, the extract of the posterior lobe of the pituitary gland loses its effect if injected while the subject is sleeping.

(*b*) Narcolepsy, Cataplexy, Gélineau's Syndrome and Pyknolepsy: It is not yet proved that these are due to lesions of the infundibulotuberal region. The need for sleep is definitely controlled by the diencephalic vegetative system, but neither this nor the appetite for food or drink can be positively ascribed to that region.

(*c*) Hyperorexia, Bulimia: It has long been known that excessive hunger is often indicative of involvement of the central nervous system. The work of Muller, Greenstein, de Castex and de Camauer have made it possible to determine the presence of a hunger center in the diencephalon.

(*d*) Polydipsia: The influence of the hypothalamus on thirst is strikingly shown by the work of the neurosurgeon. The conscious patient immediately complains of intense thirst when the surgeon touches the interior of the ventricle in this location.

(*e*) Glycosuria: Complete hypophysectomy, provided the hypothalamus is intact, does not result in glycosuria, but a mild injury to the diencephalon often brings about a delayed and prolonged glycosuria, resembling diabetes. The power of renal concentration is markedly lowered in cases of diencephalic glycosuria, and effects on the retention of chlorides are by no means exceptional, often giving rise to edema.

(*f*) Obesity and the Lipodystrophies: Simple compression of the ventricular floor brings about inhibition of sexual and bodily development with the production of obesity. In some cases roentgen examination makes it possible to differentiate adiposity due to cerebral involvement from that due to a hypophyseal disorder. Sanchez reported the existence of adiposity in which the mamillary, supra-optic and paraventricular nuclei are damaged. The type of obesity (plethoric obesity) described by Cushing appears to be always associated with an adenomatous proliferation of basophils in the hypophysis. In cases of progressive lipodystrophy the adiposis is usually localized over the lower extremities, while the trunk, arms and face may be thin. The distribution may be inverted, however. Such a condition may follow encephalitis, and this indicates the primary neural origin.

(*g*) Laurence-Moon-Beidl Syndrome: This is a condition related to the Fröhlich syndrome in which there are retardation of intellectual and somatic development, adiposity, genital atrophy and retinitis pigmentosa, often accompanied by malformation such as anal atresia and polydactylism. This is a familial condition showing some indications of involvement of the vegetative function of the diencephalon. It is different, however, from Leschke's syndrome, or pigmentary dystrophy, in which there are definite indications of endocrine disturbances.

(*h*) Adiposogenital Syndrome: This is characterized by hypoplasia of the external genitals, obesity, particularly pubic, a fine feminine skin, tapering fingers, increase in carbohydrate tolerance and often a certain intellectual deficit. Polyuria, hypnolepsy and disturbances in thermal regulation may be present. This syndrome has been produced in animals by lesion of the infundibulum. In many instances both the gland and the diencephalon have been injured, but the destruction of the pituitary gland alone brings about only mild genital atrophy. Moreover, this syndrome is rather frequently the product of encephalitis.

(*i*) Macrogenitosomia Praecox, or Pellizzi Syndrome: This is no longer thought to be caused by the excess of pineal secretion; it is apparently due exclusively to involvement of the mamillary body.

3. *Other Conditions Related to Diencephalon.*—Repercussion of Lesions of Genital Glands on Hypothalamus? An interesting case has been reported by Tapie: A soldier, injured in the genital region, three years later presented typical polyuria, polydipsia, loss of potency and atrophy of the testicles, with obesity and somnolence. Moreover, in another case of injury to the genitals a transformation in the character and a modification of the secondary sexual characteristics appeared in a man, who adopted the behavior of a woman.

(*b*) Hypophyseal Cachexia (Simmonds' Disease): This consists in premature senility, with graying and falling of the hair, loss of teeth, loss of sexual potency, progressive asthenia and emaciation. Most authors regard this syndrome as due primarily to involvement of the diencephalon.

Hypothalamus and Hematopoiesis: There is a definite relationship between the diencephalon and the function of maturation of the red and white cells. This has been proved experimentally, and in a patient with a cystic tumor of the third ventricle there appeared crises of hypnolepsy, hyperthermia and neutrophilic leukocytosis. A large outpouring of red cells, some of them immature, is occasionally observed in cases of lesions affecting this region, and possibly polycythemia is related to this condition, occurring sometimes in narcoleptic states. This polycythemia does not occur if the animal is subjected to splenectomy. It is possible also that the primary anemias are related to infundibulotuberal lesions.

Hypothalamus and Osseous and Muscular Dystrophies: Osseous and muscular dystrophies may also be associated with a lesion of the diencephalon. Most important of these is the Schüller-Christian syndrome, in which infiltration of the infundibulum is always found.

According to Curschmann, myotonia atrophica is caused by an alteration in the walls of the third ventricle. This disorder is often accompanied by obesity, lipodystrophy, polyuria and genital atrophy, but it is far-fetched to say that Steinert's disease is due to a diencephalic lesion.

Hypothalamus and Epilepsy: In regard to epilepsy, the mistake is often made of confusing the localization of the lesion with the localization of a function. A number of authors have incriminated the middle part of the diencephalon as affected in essential epilepsy, and Penfield has given a graphic description of epilepsy due to involvement of the diencephalon. It is true that many of the phenomena of the epileptic crises are vegetative; it is also clear that such paroxysms are alleviated by barbiturates, which have a rather selective action on the mesodiencephalon, and it is possible that . . . some cases epilepsy . . . origin in the diencephalon.

Hypothalamus and Psychic Disturbances: The relationship of the hypothalamus to psychic perturbation leads along the road to metaphysics toward the field of brain mythology. The personality in its various aspects, the ego and the id, intelligence, reason, instinct, etc., may have some relation to this important part of the nervous system, but such a relation is certainly not proved. A tumor growing in the floor of the third ventricle often causes transformation of character; in some cases there are even confusion, hallucinations and dreamy states, resembling the syndrome of Korsakoff. While disturbances in the region of the infundibulum can bring about such striking alterations, it must not be supposed that the diencephalon is really a psychic center or center of consciousness.

Space is lacking for consideration of vegetative disorders, such as salivary, sudoriferous, lacrimal or sebaceous secretion, arterial hypertension, peptic ulcer, etc.; there has been some work on the specificity of the various nuclei in the control of certain functions, however. It seems that the nuclei of the tuber cinereum regulate water and salt metabolism and that the paraventricular nucleus determines fat metabolism. However, the quality of the lesion seems to be of even greater importance than the exact location, the sudden development of minute lesions often being the signal for the appearance of characteristic syndromes. Moreover, lesions may be either destructive or excitatory. On the other hand, the hypothalamus may seem to be completely destroyed without the appearance of any significant symptoms. Every case should be studied on its merits, and theories should all be made subordinate to facts.

DISCUSSION

J. FROMENT: There has been a tendency to dispossess the hypophysis of most of its syndromes, but Lhermitte has been wise in restraining the enthusiasm of those who would allot all the functions to the diencephalon. Acromegaly and giantism certainly seem to be glandular syndromes, but other disturbances may be of dual origin. Undoubtedly the two structures, neural and glandular, are closely joined functionally. Psychic disturbances can certainly occur in cases of lesions of the diencephalon. Possibly some of the dreamlike states due to the dissociation of the function of sleep have an analogy in the ocular spasms of encephalitis.

SYNDROME REFERABLE TO THE INFUNDIBULUM AND TUBER CINEREUM FOLLOWING INJURY TO THE SKULL. MARINESCO, FAÇON and BRUCH.

The authors report the occurrence of a syndrome referable to the infundibulum and tuber cinereum which followed cranial trauma. The patient presented mild disorders referable to the pyramidal tract and vestibule with symptoms closely resembling those of hysteria. There were marked gain in weight, diminished libido and ejaculatio praecox, loss of hair on the face, considerable thirst and marked insomnia. During the examination there was an intense crisis, during which the face became flushed, the extremities became tremulous and a generalized convulsion occurred. Vagotonia was marked. The authors expressed the belief that a lesion was present at the base of the brain and referred to a number of similar cases.

SYNDROME OF NEURO-ANEMIA AND ALTERATIONS DUE TO INVOLVEMENT OF THE DIENCEPHALON, INFUNDIBULUM AND TUBER CINEREUM. LHERMITTE, WORMS AND AJURRIAGUERRA.

The authors observed a typical case of pernicious anemia with pronounced subacute combined degeneration and found foci of demyelinization in the globus pallidus and in the vegetative centers surrounding the third ventricle. Such lesions may underlie some of the visceral symptoms observed in cases of pernicious anemia.

HISTOLOGIC EXAMINATION OF NEUROSPONGIOMA OF THE TUBERO-INFUNDIBULAR REGION. ABSENCE OF VEGETATIVE SYMPTOMS. ANDRE-THOMAS, DE MARTEL, SCHAEFFER, GUILLAUME and TRELLES.

The authors report a case of a tumor of the infundibulum in which no vegetative symptoms were observed. While there was apparently gross destruction of these nuclei the cells were still maintained effectively. After operation there was a high rise of temperature.

STUDY OF THE DIENCEPHALIC VEGETATIVE SYSTEM BASED ON ANATOMICOCLINICAL OBSERVATION IN A CASE OF CYSTIC EPENDYMOCYTOMA OF THE THIRD VENTRICLE. DRAGANESCO and SAGER.

The authors report a case of cystic tumor of the third ventricle in which there were diabetes insipidus with lipodystrophy, disturbances of sleep, dreamlike delirium and mental disturbances.

FUNCTIONAL DISTURBANCE OF TUBERO-INFUNDIBULAR CENTERS FOLLOWING EPIDEMIC ENCEPHALITIS. MARINESCO, FAÇON and BUTTU.

The authors reported the case of a young man in whom after an attack of encephalitis there developed marked increase of weight, growth of hair over the body, increase in the size of the genitalia and intense sexual desire. Three years later the excessive sexual activity gave place to impotence, and then the parkinsonian syndrome developed. There was a myxedematous appearance with slight exophthalmos and marked atrophy of the genitals, and finally moderate diabetes insipidus appeared.

Pseudo-Encephalitic, Febrile and Hemimyoclonic Form of Cystic Glioma of the Cerebral Peduncle. Roger, Raybaud and Mosinger.

The authors report the case of a girl, aged 16, who had a syndrome characterized by fever, hemimyoclonus and, later, headache, vomiting, choked disk, constipation, change in the visual fields and progressive paralysis of the right side. The disturbances were due to a cystic glioma involving the midbrain and interbrain.

Vegetative Syndrome: Strictly Limited Hypothalamomeningitis. Ayala.

Ayala reports a case of congenital syphilis with meningo-encephalitis sharply limited to the hypothalamic region in which marked polyuria, weakness, headache, fever, hypersomnia, epileptiform crises and visual and auditory hallucinations occurred.

Is Chronic Primary Ankylosing Polyarthritis a Clinical Syndrome Depending on Alterations of the Vegetative Mesodiencephalic Apparatus? Negro.

Negro discusses the possibility that chronic primary ankylosing polyarthritis may be a clinical syndrome due to alteration of the vegetative apparatus in the middle part of the diencephalon. He bases his conclusions on the marked metabolic and vegetative disturbances occurring in patients with this disease.

Diabetes Insipidus Following Typhoid: Cure by Roentgen Irradiation of Diencephalon. Vercelli.

Vercelli described the case of a young woman in whom diabetes insipidus developed after an attack of typhoid. The condition had been present for five years. Cure followed roentgen irradiation of the diencephalic region.

Thermal Regulation and the Infundibulotuberal Region. André-Thomas.

In the evolution of vertebrates a change from the cold-blooded or poikilothermal to the homothermal animals becomes evident, although in hibernating animals and in the new-born of the latter species the law does not hold good. In homothermal animals the balance of temperature depends on thermogenesis and on thermolysis. According to the researches of Karplus and Kreidl, the infundibulotuberal region is of great importance as a sympathetic center. Stimulation of this region produces dilatation of the pupil, protrusion of the eyeballs, secretion of tears, saliva and sweat and vasoconstriction. Just what rôle this plays in thermoregulation is not clear, but the contraction of the peripheral arteries certainly cuts down the amount of heat radiated and thereby tends to control thermolysis. While stimulation or destruction of the cerebral cortex may cause some upset in thermoregulation, the localization is uncertain and the picture confused. It seems, however, that in experimental punctures the deeper the needle penetrates in the region of the third ventricle, the more profound are the results. Puncture of the basal portions of the brain is usually followed by a slight drop in temperature followed by mild fever, the temperature rising a little more rapidly in the liver than in the muscle and still later in the skin. This rise in temperature is not due to restlessness of the animal, because it occurs when curare has been administered. Either after a section between the thalamus and the inferior colliculus or after extirpation of the anterior and intermediate portions of the brain the rabbit can no longer regulate its central temperature and becomes poikilothermal. Simple separation of the anterior from the middle portion of the brain, however, does not modify thermal regulation. The thermoregulatory centers therefore seem to lie in the posterior two thirds of the midbrain centrally and medially, and they do not include the mamillary bodies.

Keller and Hare reported that median section of the hypothalamic region produced thermal disorders that lasted for three months after operation. Chilling

caused a drop in central temperature, while polypnea and vascular dilatation still appeared under the influence of heat. Leschke showed that destruction of the tuber cinereum brings about high fever, rapidly fatal, and Bremer, on the other hand, showed that a drop in temperature at times results from a similar lesion. The latter expressed the belief that obesity due to involvement of the hypophysis, characterized as it is by a low basal metabolic rate and low temperature, is probably due to chronic mild lesions in the thermal center of the tuber cinereum. Bayett, Alpers and Erb considered the infundibulum of prime importance for the regulation of body temperature. The body temperature can also be controlled by the temperature of the blood going through the brain; chilling the carotid arteries causes a reflex rise in central temperature, while warming it produces dilatation of the peripheral vessels and a fall in temperature. Hashama found that a small space, 2 or 3 mm. lateral to the midline in the tuber cinereum, inhibits reactions caused by warming or chilling; hence that center is regarded as the location where this reflex action is initiated. The center also seems to respond in a different manner to various drugs, which exert either a general action on the tonus of the sympathetic or parasympathetic nervous system, or a direct action on thermoregulatory centers. The fact that injection of bacterial poisons does not produce a rise in temperature when the infundibulum has been destroyed has been observed by many authors. Moreover, the importance of the thyroid and adrenal glands is shown by the fact that certain substances do not produce fever after the removal of these glands, although the fever may reappear after the injection of thyroxin. Direct action of certain chemicals on the wall of the ventricle is variable, phenol, potassium and sodium, for instance, among others, producing a rise in temperature with sweating whereas magnesium and calcium inhibit such a reaction. Washing the fourth ventricle with an acid solution increases the respiratory rate, the heart rate and the secretion of sweat and produces an elevation of temperature, whereas washing it with alkaline solution produces the opposite effect. These reactions can also be obtained when the cerebral peduncle has been sectioned, and all repercussion that may occur in the superior centers is inhibited. The infundibular region is particularly sensitive to the local action of pharmacodynamic agents.

Pathologic studies are less precise than experimental ones because of the difficulty of excluding processes outside the central nervous system. It is known, for instance, that a lowering of the temperature may cause the appearance of disease, whereas a rise of temperature increases the resistance to infection. Tumors of the brain offer the most precise data on the relation of the hypothalamus to thermal regulation. Strauss and Globus have reported three cases in which an elevation of temperature was associated with the presence of such a tumor, and reports of many others are found in the literature. The fever is apt to be irregular, and the peaks do not correspond with the peaks of the pulse rate, a condition also found in tuberculous meningitis. Crises of hyperthermia with marked increase in the leukocyte count are also sometimes observed. The febrile reaction following operative intervention on the brain, the bête noire of surgeons, is a common manifestation and occurs too early to be explainable on the basis of an infectious process. That these crises are due to an elevation of the central temperature there is no longer any doubt, and the fact that antipyretic action on the center can bring down the temperature is of significance. The fever is particularly likely to occur when there is an abundant loss of cerebrospinal fluid, and such accidents are less frequent when the ventricle has been punctured twenty-four hours before the operation. In view of the absence of other phenomena, it is probably better to term this elevation of temperature hyperthermia rather than fever. Thermal disturbances in epidemic encephalitis are frequently observed and appear to vary according to the localization of the infection. Sometimes there is a low degree of fever; sometimes there are attacks of hyperthermia appearing for a long period; sometimes there is inversion of the thermal rhythm, and sometimes there is a permanent mild hypothermia. The injection of solution of posterior pituitary into the third ventricle causes a pronounced fall in temperature, which may reach 5 F. Pilocarpine has the same effect. These drugs act on the parasympathetic system, whereas pitressin and

pitocin cause no reaction and atropine or avertin counteract the action of posterior pituitary and pilocarpine. The injection of air into the ventricles, either directly or by the spinal route, often brings about fever and sometimes leukocytosis. In most cases it is impossible to say whether the reaction on the thermoregulatory process is of excitatory or inhibitory nature. This is particularly true since a disturbance of the balance between thermolysis and thermogenesis may occur in either direction. Moreover, in a majority of cases of lesions of the hypothalamus disturbances in temperature are probably little if at all evident, and it is impossible for either the physiologist or the clinician to establish a topographic atlas of the disorders of the vegetative system in relation to the known cellular units of the hypothalamus. The phenomena observed during operative intervention on or near the floor of the third ventricle are extraordinary; one patient complains of thirst and another of hunger, another breaks out into a sweat, another vomiting, another falls asleep, and so on. All these reactions seem to indicate that the floor of the third ventricle is a crossroads of first importance, where the needs of the organism arise, some manifesting themselves as conscious, and some as unconscious, impulses. Many of these impulses, moreover, are at once neurochemical and physicochemical, and they probably act through different mechanisms on the body as a whole. It should be recognized that at the present time most of the observations indicate the probability rather than the certitude of the presence of a tuberal or hypothalamic center for thermoregulation. The juxtaposition of thermal disorders and other vegetative disturbances in the pathologic involvement of the infundibulum confers an undeniable value on this region and indicates that the infundibulotuberal region has an important part to play in the general anatomic and physiologic plan of thermoregulation.

THERMOREGULATORY PROPERTIES OF THE TUBER CINEREUM. ALBERT SALMON.

The sympathetic and the endocrine system are the principal regulators of thermogenesis. The thyroid hormones activate organic oxidation, whereas hypothyroidism and thyroidectomy are usually accompanied by marked hypothermia. Menstrual hyperthermia is supposed to be due to hyperfunction of the ovaries. According to most authors, epinephrine raises the temperature, particularly if it is injected into the ventricles. Disease of the adrenal glands, however, produces hypothermia, which is a grave and common symptom in Addison's disease. Insulin also tends to bring about hypothermia, which is decreased by administration of epinephrine. The temperature falls after hypophysectomy, and hypothermia is one of the principal signs of Simmonds' disease. The hyperthermia which follows the injection of solution of posterior pituitary is one of the best diagnostic signs of a hypophyseal lesion, according to Cushing. Thrusting a needle into the tuberal nuclei does not produce hyperthermia in animals whose adrenal glands have been removed, but hyperthermia occurs in such animals after grafting of adrenal tissue. These facts indicate that the thermogenic properties of the tuber cinereum are attributable in part to, or at least are reenforced by, the adrenal secretions. Moreover, the febrile chill with its shivering is linked closely to the hypersecretion of epinephrine produced by irritation of the tuber cinereum. The reverse action, the effect on the glands of a fever, has also been noted; for instance, hypertrophy of the hypophysis has been known to occur in cases of infectious diseases, and adiposogenital dystrophy is said to have been nearly completely cured by means of fever therapy. During the fever there is retention of water and salts, and the temperature falls when fluids are expelled. Should dehydration occur, however, the temperature may again rise. Hyperfunction of the posterior lobe of the hypophysis produces retention of fluid and edema that disappear after roentgen irradiation of the gland. In summary, Salmon expresses the belief that the thermoregulatory properties of the tuber cinereum lose much of their obscurity when one keeps in mind their vegetative, sympathetic nature and, on the other hand, the intimate functional relationship between this nucleus and the endocrine system, particularly the hypophysis and the adrenal glands.

THERMAL DISORDERS AFTER OPERATION ON THE BRAIN. PROBABLE RÔLE OF THE TUBERO-INFUNDIBULAR REGION. DE MARTEL and GUILLAUME.

Of all the factors that seem to enter into the production of fever following operation on the brain, intraventricular pressure appears to be the most important. The picture is well established, and usually death results if it goes beyond a certain point. If a ventricle is punctured when the hyperthermic process is becoming evident a fairly large quantity of fluid under considerable pressure is often removed; after this the temperature falls rapidly, and in favorable cases the patient regains consciousness and the temperature becomes stable. However, from six to eight hours later hyperthermia may again occur, and renewed punctures have only a temporary effect, the patient dying with hyperthermia. Permanent drainage of the ventricle and subarachnoid space has made it possible to avoid certain of these complications and has made it obvious how important it is to maintain the ventricular pressure at a normal level. De Martel and Guillaume state that in carrying out this constant drainage they have been impressed by the fact that during the two days following operation there is an enormous increase of the output of cerebrospinal fluid—from 300 to 500 cc. in twenty-four hours. If the drainage becomes blocked for any reason, fever is likely to return, but if the obstruction can be removed a gush of fluid ensues and the temperature returns rapidly to normal. Even by the injection of air under increased pressure, hyperthermia can be produced, but if the pressure is allowed to fall, hyperthermia is largely avoided. One demonstrated experience was that in which the ventricles were narrow and difficult to locate and several punctures brought forth no response; no fluid was withdrawn. The temperature rose rapidly to 40 C. (104 F.), and the patient was deeply comatose. The ventricle was then punctured, and 60 cc. of fluid was removed; the fluid was under increased pressure. An hour later the temperature was practically normal, and the patient was conscious. Hyperthermia is observed particularly in cases of obstruction of the posterior orifice of the aqueduct of Sylvius. In such cases, even though decompression of the lateral ventricles is performed before the obstruction is completely removed the removal of the obstructing agent causes a flow of fluid, and often there is a rapid rise of the body temperature. In certain cases from eight to ten days after operation there may be a rise of temperature, which indicates that ventricular obstruction has occurred; the condition is then quickly relieved by drainage of the ventricles.

Marked phenomena are likely to result from the attack on a tumor in the infundibular region, particularly a cyst of Rathke's pouch, and rather brusk changes in temperature may occur immediately after the exposure and incision of the capsule of the tumor. However, just as rapid falls may occur after the rise without being accompanied by any peripheral vasomotor disturbance or sign of intraventricular hypertension. They are probably due to direct irritation of the thermoregulatory centers in the tuber cinereum.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

March 21, 1935

C. A. MCDONALD, M.D., *President, Presiding*

THE EVOLUTION OF PUNISHMENT. DR. A. WARREN STEARNS.

The individual man when annoyed by the conduct of others instinctively retaliates; thus he reacts as if there were a punishing propensity. Human beings tend to conventionalize and ritualize their necessities; thus punishment becomes a custom, and institutions are set up for its administration. Man also tends to sanctify customs arising from individual necessity or social need.

Savages pay little attention to individual quarrels but punish violations of tribal customs. This is done to propitiate or reward good and bad spirits. In archaic civilizations the same procedure was carried out; there was some formalization of individual quarrels, and the religious component of group punishment was extended. Government intervened, at first for the purpose of preventing excessive retaliation. The elements of duty and purification were developed, and a punishing class was established whose zeal became an added factor.

In the classical civilizations there was a tendency to settle individual quarrels by composition. Punishment by society was further elaborated and formalized, and to religious obligations were added governmental duties.

The punishing class was extended during feudal times; the divine right of rulers gave society occasion for further control of individual quarrels, and more elaborate conventions were set up for their settlement. Religious obligation and social betterment were still important factors, but the theory of the deterrent effect of punishment was a step toward social sanitation and the individual person was punished as an example, so that society would be better. This led to an increased severity of punishment and brought the punishing class into greater importance.

During the eighteenth century, as part of the revolt against the feudal system, there appeared the humanitarian motive, and for the first time attempts were made to treat the individual offender. At first this treatment consisted of religious efforts; then formal education was offered as a cure, and from this gradually developed the modern idea of reformation. Thus the punishing formula for purposes of social sanitation was continued and the treatment of the individual offender elaborated.

In the latter part of the nineteenth century studies of individual offenders were begun. These studies were at first anthropometric and later became psychiatric. From this has developed the present-day system of obtaining case histories. Thus, at the present time there is still the punishing propensity of human beings, conventionalized and ritualized by organized society.

I am at present engaged in extending the application of scientific methods through case histories and social service technics. Resistance to this comes because of a universal difficulty in changing established customs and because of the dominance of the punishing class. If one is to advance one must condition the punishing propensity of individuals and must substitute for the punishing class a professional group interested in social sanitation and individual treatment.

DISCUSSION

Dr. J. Loman, for Dr. A. Myerson: While punishment may be defined as arising from the natural social reaction of the praise, blame, reward and punishment complex, it is as natural as the physical reflexes and belongs to the organizing and organized structure of human life. It becomes ritualized and ceremonialized as all other habits and functions of the individual do, and, furthermore, as Dr. Stearns pointed out, it falls into the hands of specialists, just exactly as cooking and medicine become specialties. The specialists develop ideas. They enhance their own importance and also, consciously or unconsciously, use punishment as part of their own power and to maintain the social structure as they believe it should be maintained. Naturally, punishment becomes linked with cruelty and sadism and, to a certain extent, expresses the latent cruelty and sadism of the community and of the individuals who carry out the law.

However, this is not the whole story. Along with the tendency to punishment in human life, there is the gentler trend toward pity and toward reform. However feeble these may be, they are constantly existent, and, furthermore, they too have had their specialists—men who have believed that the salvation of the world and of the individual man rests on the use of love and pity. Consequently, there arises a double stream of attitudes toward offenders—punishment and pity. Pity and tenderness have gradually increased in scope through historic periods. The attitude toward the offender has notably softened. One can trace, even within the last hundred years, an enormous enhancement of the power of this set of

impulses. Cruelty in its personal individual relationships has notably decreased. Punishment no longer is so stark and mutilatory and is not so directly given over to the infliction of physical pain.

However cruel it may be to imprison a man for life and to shut him off from his fellows for a longer or shorter duration, it does not involve that lust for punishment which is involved by cutting an arm off, branding with a hot iron or the use of the lash. This greater tenderness and lesser drive toward definite mutilatory painful procedures is evidenced in the army and the navy, in the relationships between parent and child, in the sexual field and in the relationship between master and servant, as well as in the attitude toward crime.

More important still, there has gradually arisen a technic which has attempted at least to do away with the entire social attitude of praise, blame, reward and punishment. In other words, it seeks to estimate and evaluate whatever it deals with in objective terms and without emotion. That is science. The scientific procedure is an effort, at least until the idea of indeterminism came to eliminate, to bring an act or deed which is punishable into an etiologic relationship. In a certain sense it is deterministic, and as such it divorces itself from ideas of horror, loathing and those emotional responses which lead to punishment. Punishment may be given under a scientific attitude, on the basis that this alters conduct and is a deterrent to crime; as such, punishment is legitimately a scientific instrument.

However, the whole attitude of science, which has gradually and slowly encroached on the attitude toward crime, is aloof from punishment as expressing the emotions of the group or of those individuals who are to deal out the punishment. The basic approach of science is that conduct of any kind constitutes a phenomenon; if that is true, laws can be discovered which explain the occurrence of these phenomena. Its weapon is research, and its technic that of all science, namely, studying various types on a hypothesis and testing them out against the facts analyzed by statistics. The final weapon of science is experimentation. This, of course, is difficult to bring into human relations and to utilize for the study of human conduct. Nevertheless, it is the final and most valid instrument of proof.

DR. A. H. HARRINGTON: Dr. Stearns has evidently studied the Bible and tells how the old Mosaic law, as set forth in Deuteronomy, exhibits the motive of punishment. In dealing with offenders in the legal aspect, society has been pervaded with this motive of the old Mosaic law for centuries. Since the seventeenth century the law has striven to eliminate the demands of society for vengeance as exhibited in retributive punishment. Marked progress in such procedures has been made during our own time, particularly relating to offences committed by mentally diseased persons. Nevertheless, this instinctive element in the human subject to inflict a punishment, to find a scapegoat and to relieve emotional tension in the face of some monstrous or revolting act becomes a tremendous force. For instance, Guiteau, assassin of President Garfield, undoubtedly suffered with a mental disease when he committed the act. The verdict of the jury, which sent him to execution, met with almost universal approval. There was a striking case a number of years ago in the state of New York of a priest who from earliest childhood had been very religious. As a small child he erected an altar in his home and made priestly robes for himself. He was called the little priest. As he grew to adult life, sadism and sexual perversion developed; his final act was the killing of a young girl. He had on the left side of his chest a delicate pink nevus. This was related to his belief in his identification with Christ. He went before the church altar and waited for a sign from God. The sign came. He did the act and divided the body into seven parts, which number was to him a symbol. These complexes and conflicts between his religion and his sadistic and sexual drives led to the psychosis. When he came to trial the feeling of the public was so strong that nothing could counteract it, and the man was executed. That eminent psychiatrists testified to the long-standing mental disease, and that it was shown that the man had been in a hospital for mental diseases in his own country did not mitigate the vengeful demand for punishment. There is a long way to go

yet in such an instance before all components of society are ready to accept the truths of psychology and psychiatry.

DR. W. N. HUGHES: Fortunately I have known Dr. McDonald for a good many years, and I know that he treats his medical brethren squarely and tolerantly. Otherwise, I should feel that he is satisfying his punishment propensity in selecting us to speak one after another and that he is using public opinion, which Dr. Stearns considers one of the best weapons for punishment, to do this. Before one speaks one usually has an idea in regard to what public opinion is going to do. When one speaks, public opinion acts, and after one speaks one finds out what it has done. Dr. Stearns has told how typhoid has been controlled through group sanitation rather than through control of individual cases. Yellow fever has been controlled in the same way. I should like to have him develop further his ideas in regard to how and what things can be done in controlling crime through working with the group rather than with the individual person. A few days ago I was talking to a director of a school for delinquent children in Pennsylvania, where boys are taken at 9 or 10 years of age and kept until they are 17 or 18. They are taught occupational therapy and reformed if they can be. Occasionally good results are obtained. This director found the social service department not as valuable as its workers would lead him to think. Many patients did not show responses to treatment in the way that the members of the social service department expected or talked as if they expected. Dr. Stearns pointed out that social service is one method of controlling the problems of crime. I wish to ask him if this would be through group control rather than through individual control.

DR. W. BLOOMBERG: I wish to make two points. First, as an additional and striking evidence of the tendency to immediate retaliation, the general public attitude of indignation in the recent case of the Millens and Faber may be noted. It is extremely difficult to repress the welling up of the tendency to immediate retaliation whenever behavior out of line with custom is encountered. Even among trained prison workers in a modern community prison such as Norfolk this sort of annoyance and flare-up of temper breaks out occasionally among the officers. Certainly it is much in evidence in the old time type of prison, where the entire routine is designed to produce conformity at a very low level.

The second point is in relation to the part psychiatry can play in the attempted solution of the problem of crime. The criminal who is a criminal on a neurotic basis, in the sense of Freud and Alexander, is, I think, not common. Mental deficiency and so-called psychopathic personality, too, do not play a numerically great part. The great mass of criminals in prison are "normal"; that is, they are much like a cross-section of the general population. What psychiatry can bring to the problems of these persons is the important thing, and that is a technic and an understanding insight. The modern psychiatrist is interested not only in mental disease but in all problems of human behavior and motivation, especially in maladjustments, whether they are mental or social. It is the application of the psychiatrist's technic and insight to the consideration of these problems in the "normal" criminal rather than in the smaller group of the mentally diseased that offers the fruitful field. I hope that many more trained psychiatrists will bring their training to this problem. It will result in benefit to both criminology and psychiatry.

DR. M. H. A. EVANS: The subject matter seems to have changed from the consideration of the evolution of punishment to an entirely different matter—the character of the prisoners. They have little to do with each other. There is a wide gap between the offense which the criminal sets out to commit and the crime for which he suffers punishment, and in that gap is the very important distorting agency which is called the trial. It is the trial which envelops the illegal act in such a smoke screen that the prisoner may be found guilty of something quite different from the offense he originally intended to commit.

Thus, a person wishing to avenge a wrong takes a gun and tries to kill another. If he does so he is tried for murder—the greatest of offenses. But if he does

not happen to shoot where he aimed and his victim is only wounded and recovers, then his poor marksmanship saves him from being a murderer, and he may be tried for a lesser crime such as "assault with intent to kill" or perhaps "assault with a dangerous weapon." Perhaps he does not hit his intended victim at all, and then, of course, there is no assault, but he may still be tried for unlawfully discharging a firearm.

Thus, the same act with the same degree of wickedness behind it may send a person to death in the electric chair or to jail for thirty days. And this wide difference in penalties depends on the chance of a hit or miss gunshot.

The point I wish to make is this: Until crimes themselves are classified according to some moral or psychologic standard and according to the state of mind out of which they spring, and until penalties are imposed which are consistent with the criminal intent which prompted the crime, no rational classification of criminals is possible. Unless criminals are scientifically classified, psychoanalytic results can hardly be evaluated.

DR. LEO ALEXANDER: In recent years a new panacea for preventing crime has been suggested by various eugenic groups, namely, the sterilization of criminals of the present generation. There is considerable justified doubt, however, whether criminality really is a biologic and therefore an inheritable character. It appears more likely that criminality is due to a great number of criminogenous factors, many of them not biologic in nature. It would be valuable to hear Dr. Stearns' views on this matter. The literature contains little actual information as to the pedigrees of criminals.

DR. A. W. STEARNS: Dr. Harrington has illustrated the persistence of the punishing propensity, yet in certain cases this is conditioned. For instance, a while ago a bootlegger attempted to make a sale of a gallon of alcohol to an employee of mine. The employee's wife objected, whereon the bootlegger fell on her and gave her a terrible beating. I was naturally much irritated, and my punishing motive reached the maximum. Every attempt was made to protect this man from just retribution. Each time his case was reached in the lower court it was put back on the bottom of the pile in an effort to wear out the witnesses. The same procedure took place in the higher court. At last the man was sent to jail—a great satisfaction to me. On his discharge I saw him coming into my yard one day. My old animosity and resentment was aroused, especially since I thought at first that he was drunk because of his irregular movements and staggering gait. However, as he came nearer to me I recognized the symptoms of Huntington's chorea. It then came to my mind for the first time that I had had his father as a patient in the Danvers State Hospital with Huntington's chorea about twenty-five years ago. Immediately my animosity was turned to sympathy, and I have continuously felt sympathetic toward the man since.

It is difficult to say whether persons taking part in punishment are really punishing themselves. I have fancied in certain cases that there was a relation in punishing sex offenses between the punisher and the punished. However, I could never be sure whether the individual person involved was punishing himself or a rival. There is certainly a feeling of satisfaction to the punisher. I recall the morning after Sacco and Vanzetti had been executed. There seemed to be an apparent feeling of satisfaction on the part of those members of society who had favored their execution.

Concerning the possibility of discovering laws of social sanitation, I shall give as an example the diminution of burglary, at least the old-fashioned house-breaking type of burglary, by the control of the pawn-shop; also the limitation of immigration has reduced the murder rate in Massachusetts from 4 to as low as 1.2 per hundred thousand.

I have been somewhat lukewarm about psychotherapy because it has been offered as another panacea. During the Revolutionary War there was an enormous number of deaths from typhus, and physicians at that time said this was due to the shortage of cinchona. So I have been inclined to attribute unsatisfactory condi-

tions in penology to lack of psychiatry. It is hardly possible to evaluate social service technic as a therapeutic agency because it has rarely been tried under satisfactory conditions. One probation officer near Boston has had over 900 cases to supervise. I do not suggest social service technic as a panacea or cure for crime, but believe that adequate supervision in a community of known offenders would reduce crime tremendously at a much less cost than prison maintenance. It is true that social workers have many of the weaknesses of human beings in general and so are apt at times to show a bias for or against a prisoner.

Certain philosophers have objected to calling criminology a science because of its relative inexactness. This is a matter of no consequence. I wish to suggest a question. Is it possible for society to formulate and premeditate rational changes in social custom, or is one forever to be carried along blindly by instincts and customs? Up to the time when Massachusetts was settled, there had been little change in the social customs relating to crime. Deuteronomy was still the rule as late as 1692. Evil spirits were exorcised in Salem by hanging witches. However, the last 300 years have seen tremendous changes. Imprisonment as a means of punishment is an entirely new custom. In the early days of Massachusetts it was considered wicked to make too vigorous an attempt to cure disease. It will be recalled that a bomb was thrown in Cotton Mather's room when he advocated inoculation against smallpox. Prior to the Revolution little interest was found in the sick, the poor or the bad, but at this time humanitarian feeling was popularized, at first in minority groups. Most of its expression was in small societies or boards of trustees. This method gradually disappeared in favor of governmental control. For this reason individual persons often lack a sense of responsibility. When I was younger this society took an active part in such matters. I well remember the influence which the energy and sagacity of Dr. Henry R. Stedman had when he went to the state house, often as a representative of this society. Today people are inclined to leave the whole matter to officialdom. A group such as is represented in this society ought to be continually expressing intelligent sentiment in support of those who are trying to change human customs to the advantage of society.

CHICAGO NEUROLOGICAL SOCIETY

Regular Meeting, March 21, 1935

THEODORE T. STONE, M.D., *President, Presiding*

CHORDOTOMY: PRESENTATION OF A CASE. DR. ERIC OLDBERG.

Gastro-enterostomy for scirrhous carcinoma of the stomach was done on a man aged 69 two and one-half years before this presentation. At present there is evidence of abdominal carcinomatosis, and there is a large painful metastasis in the epigastric abdominal wall. Before admission to the hospital the patient had been gradually becoming more and more uncomfortable because of abdominal pain and because of the lesion, which had nearly eroded through the skin of the epigastrium. Morphine had been necessary several times in each twenty-four hours to permit any rest.

Fifteen days ago bilateral spinothalamic chordotomy was performed at the level of the fourth dorsal segment. It produced hypalgesia up to the sixth dorsal dermatome and completely abolished the pain and the need for narcotics. There was no concomitant disturbance of the sphincters. The patient is steady in walking. He has gained a little weight since the operation.

My purpose in presenting this patient is not to illustrate a favorable result of a well known operative procedure, but to call attention to the fact that chordotomy is still a good method of effecting relief from intractable pain. It is my opinion that the present furor regarding intrathecal injection of alcohol and the

simplicity of that maneuver are going to lead to serious difficulties in the hands of the general physician. There is no doubt that subarachnoid injection of absolute alcohol does work satisfactorily in certain selected cases, and there is no question that there are cases in which it is indicated. I feel strongly, however, that it takes much clinical experience and special knowledge to evaluate the method by which any particular patient with intractable pain should be treated.

DISCUSSION

DR. LEWIS J. POLLOCK: I have had no experience with injection of alcohol subdurally. The history of injections of alcohol leads me to view with suspicion the introduction of alcohol into the nervous system. The work of Schwab and Allison in treating persons with athetosis and spasticities by the injection of alcohol into the peripheral nerves may be recalled. I have, I think, 20 patients now residing in the Oak Forest Infirmary who have permanent paralysis as the result of such treatment at my hands.

I should like to see even a more critical reluctance in the use of injections of alcohol in parts related to the central nervous system, for it seems to me that any fat solvent must produce damage to the spinal cord. It may not be immediately discernible, but later the cord may not respond as well in its mechanism of defense and function as the normal cord. I should certainly discourage the use of subdural injections of alcohol for relief from pain.

I wish to ask what kind of pain resulting from visceral disease would be stopped by chordotomy. Is it the type of pain which is the result of reflex peritoneosensory impulses, or is it the type of referred pain that is mediated partly through the sympathetic nervous system? If so, it is difficult for me to understand how chordotomy stops the pain. If not, how does one differentiate the types of pain so that the indication for operation is determined?

DR. ERIC OLDBERG: Neurologists agree about using caution in the intrathecal injection of any irritating and destructive substance. That alcohol works well in some cases there is no question, and I have used it in 8 cases myself with almost uniformly good results. However, I cannot rid myself of the thought that the reason it works is that it destroys tissue, or at least renders it physiologically incapable of functioning, and that if it is given to a patient with a long life expectancy there may be subsequent difficulty from adhesive arachnoiditis, etc.

As to the pathways for visceral and somatic pain, and the type suffered by this patient, I imagine that the pain is mostly peritoneal and in the abdominal wall. In carrying out chordotomy on a patient with visceral pain, I try to section deeply enough to catch a bit of the anterior gray column, since visceral pain is thought to ascend in this region.

LOSS OF THE PUPILLARY LIGHT REFLEX FROM LESIONS IN THE PRETECTUM. DR. H. W. MAGOUN (by invitation).

In order to investigate further the relationship of the pathway of the light reflex to the pretectal region of the brain (Ranson, S. W., and Magoun, H. W.: ARCH. NEUROL. & PSYCHIAT. **30**:1193 [Dec.] 1933) the effect on the light reflex of lesions in and near the pretectal region has been studied in the cat. Large bilateral lesions of the pretectal region completely and permanently abolished the pupillary light reflex. Some damage to the caudal portion of the thalamus and to the rostral portion of the superior colliculus was unavoidable in producing these lesions, but after widespread destruction of the caudal part of the thalamus or of the superior colliculus, which left the pretectal region intact, the light reflex remained normal. It is clear that the pupillary light reflex is mediated exclusively through the pretectal region.

Unilateral lesions of the pretectal region produced a slight impairment in the pupillary reactions from lighting the ipsilateral eye and a marked impairment in the pupillary reactions from lighting the contralateral eye. While each side of the

pretectal region receives light reflex impulses from either retina, in the cat those from the contralateral eye predominate.

Destruction of the posterior commissure midsagittally caused a reduction but not an abolition of the pupillary light reactions, indicating that the pathway of the light reflex undergoes a partial but not a complete central decussation in the posterior commissure.

Miosis of short duration, apparently due to irritation, followed lesions in the caudal part of the thalamus, pretectal region or superior colliculus. In their chronic stage these lesions had no miotic effect, and in the case of lesions of the pretectal region the pupils were widely dilated, owing to the obliteration of the pupillary light reflex. Subsequent interruption of the peripheral pathway for pupillodilatation (by bilateral cervical sympathectomy) in the latter animals did not produce a miotic pupil.

DISCUSSION

Dr. S. W. Ranson: It should be emphasized that the miosis in these animals was very transitory, in most instances lasting only twenty-four or forty-eight hours, and was evidently a result of the irritation produced by the electrolytic lesion. As Dr. Magoun said, it is not safe to draw conclusions from these experiments for the interpretation of the miosis in the Argyll Robertson pupils.

Another interesting phenomenon in these cats was hippus, which occurred regularly after destruction of the pretectal region. This did not appear until after the miosis had disappeared and the pupils had become widely dilated. It is interesting that hippus occurs only when the lesions involve the pretectal area and not when the lesion involves the thalamus, nor does a lesion in the superior colliculus produce hippus. There is no satisfactory explanation for its occurrence. It seems to be something particularly relating to the pretectal region, and it is possible that the destruction of this region may remove a control from the sphincter nucleus of the oculomotor nerve which allows this nucleus to be more readily acted on by impulses from other sources.

Injuries to the Spinal Cord. Dr. Adrien Verbrugghen.

Dr. Verbrugghen showed lantern slides which illustrated his reasons for saying that fracture dislocation of the spine with injury to the spinal cord practically never demands urgent surgical intervention.

DISCUSSION

Dr. Eric Oldberg: I wish to add one more possible indication for laminectomy which I feel to be important, that is, the presence in a few hours of advancing neurologic signs. Every resident physician in a hospital should be instructed to make an immediate reasonable neurologic examination on admission of the patient. I know of nothing more disturbing than to be called to see a patient with complete paraplegia twenty-four hours after injury to the cord and to be told vaguely that the resident physician "thought the patient could move his legs a little" the day before.

Dr. Lewis J. Pollock: First, I think that the clinical descriptions of the slides are representative of a certain group of cases. I think that Dr. Verbrugghen was referring to the more severe lesions to the spinal cord. I do not think that he meant to imply that all cases of injury of the spine, even with severe injury to the spinal cord, result in the three phases of shock, automatism and death. Of course that is the syndrome observed in complete transection of the cord or in very severe lesions. I have never observed an automatic bladder in the sense in which that term is used by Head and Holmes, except in persons with very severe lesions.

I was interested in the discrimination in favor of the anterior roots as opposed to the posterior roots in recovery from lesions of the cauda equina.

During the World War, I had occasion to see patients in France with very extensive lesions of the cauda equina, with complete paralysis and extensive loss of sensation, and then to see them again many months later in America with very marked, at times almost complete, motor and sensory recovery. In the cases of severe lesions I believe that degeneration had occurred in the distal segment. For that reason I am interested in the possible functional regeneration of the posterior roots in man.

I am also interested in the treatment of the bladder, for I note that Dr. Verbrugghen puts catheterization first. In my experience with surgeons—there were not many neurosurgeons during the World War—catheterization was placed last. Plaggemeyer has written a philippic against catheterization, based on extensive experience. He thought it much better to gain the confidence and cooperation of the patient and to wait for the overflow or automatic emptying of the bladder. I have never heard of rupture of the bladder from such a course. I think that it is believed that suprapubic cystotomy is preferable to catheterization, even if the latter is very carefully followed out.

As to indications for operation, I should say that if one has evidence under roentgenographic study of spicules of bone or foreign bodies within the canal or evidence of compression of the spinal cord, whatever may be the cause, operation is indicated. In dealing with lesions of the cauda equina it is safe to wait from ten to fourteen days to observe how badly the nerves are injured by examination with electrical stimuli before deciding to operate.

One thing should be said of increased signs following injury, and that is that these increased signs must occur within a certain time limit, for one knows that in many cases of partial injury to the spinal cord necrosis may occur two weeks later which, of course, does not improve with any sort of intervention.

Dr. Percival Bailey: In the first case of injury to the spinal cord for which I was personally responsible I decided to let the bladder overflow. Instead of overflowing, it ruptured. At necropsy no obstruction to the urethra was found. Since then I prefer to catheterize the patient repeatedly if it seems that the retention will be transitory, or to insert an inlying catheter. Suprapubic cystotomy is very messy, and I try to avoid it if possible.

In certain clinics it has seemed to me that relatively too much attention is paid to the lesions of the bone. A great deal is written about the deformity of the spine and methods of correcting it by hyperextension. That is proper in many cases, but whenever there is extensive loss of sensation such treatment is likely to result in serious bed sores. I have seen patients who have been put up in hyperextension casts, and serious sepsis resulted. In trying to correct a deformity of the spine one should be careful that one does not inflict on the patient more serious injury. Other patients I have seen have been operated on long after the injury by orthopedic surgeons in an attempt to correct the spinal deformity. In certain cases the result has been complete paralysis and death of the patient. One should, therefore, be careful not to overestimate the incapacity due to the spinal deformity. The neurologic symptoms are much more serious for the patient and should be considered first.

Dr. Meyer Solomon: I wish to know what use Dr. Verbrugghen makes of the Queckenstedt test. Personally, I have been governed by the rules laid down by Mixter in his chapter in Lewis' "Practice of Surgery" (1932, vol. 12) in which he stressed the use of the Queckenstedt test for the determination of partial and complete block, and its value from the therapeutic standpoint. Mixter divided the cases into early and late, the early cases being those occurring in the first forty-eight hours, and especially those occurring in the first twenty-four hours; he contends that if there is block it should be relieved in this early stage. In the late stage it is usually too late to relieve the block, unless it is accompanied by increasing signs and symptoms or occurs very late, as a result of callus formation. Mixter thus used the Queckenstedt test as a means of determining the advisability of laminectomy.

DR. ADRIEN VERBRUGGHEN: I did not make myself clear as to the type of injury about which I was talking; it was the type resulting in paraplegia. The lesion of which Dr. Pollock spoke was rather the mild lesion which disappears rapidly, sometimes in forty-eight hours, sometimes in a few days, so that within a few weeks the patient has recovered. I purposely left cases of this type out.

I also left out increasing signs mentioned by Dr. Oldberg as they are very rare. The increasing signs are usually, I think, due to hemorrhage, as he said, and in that case the lesion should be explored immediately, for hemorrhage is something that surgical measures can do something about. If the signs are due to damage of the central nervous system, however, surgical intervention has nothing to offer, for the nervous system does not regenerate. The total damage to the cord is present at the instant of impact and not later. Why the posterior root does not regenerate is a little too profound for me. I suppose they could regenerate, but whether they could find the fibers with which to establish a synapse is rather doubtful.

As to the use of catheters, there is a bugaboo about catheters. What I intended to make clear was that the indwelling catheter should be used in the first place. There is no such thing as putting in and taking out catheters in cases of injury to the spinal cord, for that is the surest way to cause severe sepsis. The indwelling catheter is put in, irrigated twice a day and changed every five days. The urine is kept acid; methenamine is given, and it is possible in that way to keep the sepsis down to a minimum which does not injure the patient. The overflow system has a great deal against it. I have never seen a satisfactory way to manage this. There is always soiling of the bed; the patient has to be changed and moved about frequently, which is bad for his original injury and bad for the skin. The worst of all is the pain. The patient lies there gritting his teeth against the pain of the distended bladder, which is a pain I cannot minimize.

Concerning Dr. Bailey's comments, there is not much I can say except to thank him for agreeing with me in some of these things.

In regard to the spinal block that Dr. Solomon mentioned, I do not make much use of this in the early hours. I keep the patient as comfortable as possible and wait until something definite is present. I do not believe in rolling a patient over and putting in a needle to see whether I will get bloody fluid until something occurs that indicates that an effort directed toward the spinal cord is likely to meet with success.

Another type of paraplegia occurs late, as a result of the formation of callus in the spinal cord. The patient after having recovered the use of his legs begins to become progressively worse from two to six months after the injury. These patients would benefit by laminectomy and opening the subarachnoid space. In neurosurgery, so far as I know, one of the principal considerations is the obtaining of a free flow of spinal fluid.

ASYMMETRY: UNILATERAL ATROPHIES AND FACIAL HYPERTROPHY: REPORT OF CASES. DR. MABEL G. MASTEN, Madison, Wis.

This paper will be published in full, with the discussion, in a later issue of the ARCHIVES.

Book Reviews

Das Zentralnervensystem der Tiere und des Menschen dargestellt in photographischen Abbildungen. By L. Jacobsohn-Lask. Price of Parts I and II in carton, 80 marks; Part III in carton, 80 marks. Pp., Part I, 20 (text), with 163 illustrations; Part II, 38 (text), with 271 illustrations; Part III, 85 (text), with 437 illustrations. Privately published by the author at 11 Mittelstrasse, Berlin-Lichterfelde, Germany, 1935.

These exquisite photographs of nervous organs and tissues were made by the author, chiefly from his own preparations, during a period of forty years, first to illustrate his lectures at the University of Berlin; later many others were added and the whole collection assembled for distribution in partial fulfilment of the program begun by the publication, with Flatau, of the first part of the "Handbook of Anatomy and Comparative Anatomy of the Central Nervous System of Mammals" (Berlin, 1899). Jacobsohn-Lask (under the name of L. Jacobsohn) is well known to neurologists through previous publications, notably "Die Kreuzung der Nervenbahnen und die bilaterale Symmetrie des tierischen Körpers," published in Berlin in 1924 (reviewed in the ARCHIVES OF NEUROLOGY **13**:678, 1925). With Flatau, he edited for many years the *Jahresbericht über die Leistungen und Fortschritte auf dem Gebiete der Neurologie und Psychiatrie.*

The present work is an atlas of photographs with descriptions of the figures and a brief discussion of general topics. All the illustrations are photographic prints made directly from the negatives, not process reproductions. The work is in five parts, three of which are now ready for distribution. Part IV, "Inner Architectonic of the Brain Stem and Cerebellum," and Part V, "Inner Architectonic of the Central Ganglia and Cortex," are still unpublished. The three parts now issued comprise photographs of gross preparations and microscopic sections prepared by a variety of methods with unusual technical care and skill.

PART I (*Nerve Cells, Nerve Fibers, Neuroglia, Sense Organs*).—The elements illustrated are human and comparative, and the text includes a critical review of the structure of the nervous elements of vertebrates.

PART II (*Spinal Cord*).—The figures illustrate human and comparative embryologic and adult structure and nervous elements from fishes to man. The text contains a comparative survey of these structures, with a critical discussion of their significance in functional evolution.

PART III (*Invertebrates, Embryology and External Form of Vertebrate Brains*). —The text includes brief descriptions of the figures and a discussion of the phylogeny of the vertebrate brain and morphogenic principles.

The Adolescent in the Family: A Study of Personality Development in the Home Environment. White House Conference on Child Health and Protection, Report of the Subcommittee on the Function of Home Activities in the Education of the Child, E. W. Burgess, Chairman. Price, $3. Pp. 464. New York: D. Appleton-Century Company, Inc., 1934.

This report on personality development in the home environment is based on a wealth of material collected in a questionnaire study of approximately 13,000 public school children from a wide selection of cities, towns and rural communities. The children chosen were from the eighth, ninth and tenth grades. The facts brought out by the questionnnaire covered the physical environment of the home, together with the child's activities at home and his relationships with his parents. In addition, the teachers of the school grades surveyed supplied information on each child's physical handicaps, special abilities and disabilities and personality traits.

The breadth of the study and the large amount of significant material obtained make the findings of great importance for psychiatrists, psychologists and educators. The first outstanding finding is that the externals of home life, for example, the housing arrangements, are not nearly so significant for the personality development of the child as the subtler aspects of family life, such as the child's trust in the parents, affection and illness or nervousness in the parents. There is a clear tendency for the mother to play a much more important part in the child's intimate life than the father. Another interesting finding is the superiority of the personality adjustment of urban children as compared with rural children.

The specialist will be interested not only in these general findings but in the relation of personality adjustment and various specific factors, such as the type of discipline used or the sex education received. The evidence on many of these factors should be useful in the guidance of normal children as well as in weighing the effect of the many contributing difficulties which appear in the histories of maladjusted children.

It is stated that the study had to be completed in nine months, and its faults are apparently the result of the shortness of time. The necessity for speed was probably the factor which led to the basing of data on parentage on the birthplace of the father; the birthplace of the mother, whose relation to the child was usually more intimate than that of the father, was disregarded. Furthermore, the material collected would seem to permit of more extensive analyses than those presented in the report. It would be interesting to know, for example, the relation between left-handedness and various factors of adjustment, and also to know more about the occurrence of special abilities or disabilities, as judged by the teacher, and their effect on personality adjustment. The faults, however, are comparatively unimportant when they are weighed against the mass of material carefully collected and reported, and the study as a whole is a valuable contribution.